

# THE EXTRA PHARMACOPŒIA

*Made and Printed in Great Britain by  
Percy Lund, Humphries & Co. Ltd., London and Bradford.*



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1941-1942**

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# PREVIOUS EDITIONS OF THE EXTRA PHARMACOPŒIA

						No. OF PAGES (excluding Introductory)
1st Edition published	..	..	..	1883	313	
2nd	"	"	..	1884	330	
3rd	"	"	..	1884	330	
4th	"	"	..	1885	446	
5th	"	"	..	1888	462	
6th	"	"	..	1890	485	
7th	"	"	..	1892	524	
8th	"	"	..	1895	580	
9th	"	"	..	1898	626	
10th	"	"	..	1901	688	
11th	"	"	..	1904	809	
12th	"	"	..	1906	1075	
13th	"	"	..	1908	1203	
14th	"	"	..	1910	1054	
Supplement: Organic Analysis	"	hart	..	1910	80	
15th Edition, Vol. I published	..	..	..	1912	1112	
15th	"	" II	"	..	370	
16th	"	" I	"	..	1113	
16th	"	" II	"	..	469	
17th	"	" I	"	..	1115	
17th	"	" II	"	..	688	
18th	"	" I	"	..	1163	
18th	"	" II	"	..	728	
19th	"	" I	"	..	1207	
19th	"	" II	"	..	759	
20th	"	" I	"	..	1216	
20th	"	" II	"	..	889	
21st	"	" I	"	..	1182	
21st	"	" II	"	..	1148	

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## PREFACE

It is a far cry from the slim volume of 313 pages which comprised the first edition of the *Extra Pharmacopœia* published by W. Martindale in 1883 to the Twenty-second Edition, of which this volume alone contains 1289 pages. The aim of the original compiler was to provide medical men and pharmacists with practical and up-to-date information concerning drugs and galenicals to supplement that contained in the *British Pharmacopœia* published sixteen years previously. The book met with such an enthusiastic reception that four editions were published in three years. From a kind of unofficial addendum to the *B.P.* there has gradually emerged a work of independent status including in its scope the whole field of therapeutics and the allied sciences. Every effort is made to include within its covers information on all the compounds and preparations which the physician uses, or is recommended to use, including notes on their composition and practical observations on the results of their application. The book also provides the pharmacist with information upon the constitution and properties of the chemical, animal and vegetable drugs necessary to the preparing of medicaments and the dispensing of prescriptions. So far as space permits the book aims at providing for the physician and pharmacist a convenient compendium of information otherwise only obtainable, in many instances, by reference to numerous text-books and by arduous searching through the scientific literature.

Almost from its inception one of the outstanding features of the *Extra Pharmacopœia* has been the breadth of its outlook not only in respect of the drugs and chemicals described in its pages, but also in respect of its sources of information. To those previously unacquainted with the book, a cursory glance through the list of abbreviations will indicate its wide scope. Every new edition of a foreign pharmacopœia is carefully searched for new substances or preparations or for important alterations. The latest developments in medicine and the allied sciences as they appear in the world scientific literature are followed, either at first-hand or through abstract journals. The continual stream of foreign proprietaries flowing into this country from manufacturing houses of established reputation is assiduously watched. It is the presentation of the essential features of this vast accumulation of material which gives the book its unique character and renders it indispensable to all physicians and pharmacists who wish to keep abreast of modern scientific development.

It was fortunate, therefore, that a great part of the material for this new Edition had been collected prior to, or within a short time after, the outbreak of hostilities in September 1939, since it permitted the book to retain its international outlook at a time when this aspect is of especial importance. To those medical men and

scientists from every corner of Europe who are now seeking asylum in this country, the *Extra Pharmacopœia* should prove an invaluable source of information. There is no other book which enables the foreign practitioner to compare the standards and strengths of drugs, chemicals and galenicals with those obtaining in his own country, or to match the proprietary preparation with which he has been familiar with a similar British product. Similarly, the many American doctors who are entering the medical services of Great Britain should find the book valuable, for it contains not only the official standards, strengths and descriptions of the *U.S.P.* and its *Supplements*, correlated with those of the *B.P.* and the *B.P. Addenda*, but in addition details of many American proprietaries which are on the market in this country. Furthermore, some thirty per cent. of the abstracts in the book are derived from American medical and scientific literature.

In spite of the fact that the stream of scientific information in Europe has been dammed at its source, it may be that little of importance to medical progress has been lost; in Germany itself all scientific research, except that having a direct application to war purposes, is probably at a standstill, and in the conquered countries the centres of learning are being closed down or reduced to a uniform level of mediocrity. Many of the leaders of scientific progress are exiles. In England and America, however, the progress of medical research, though inevitably affected by war-time conditions, has continued uninterrupted and the results of that progress up to the spring of 1941 are incorporated in this book.

Thus although this new edition makes its appearance almost two years after the outbreak of hostilities, it is no less comprehensive and up-to-date than any of its predecessors, and every worth-while development in pharmacy or therapeutics evolved during recent years has been included in its pages.

Indeed, the difficulty has been not that of finding new material, but of selecting material sufficiently out-of-date to justify omission, in order to make room for new matter demanding incorporation. In particular, it was necessary to find room for the inclusion of over two thousand new abstracts taken from the world literature during the past four years. In the earlier editions, when the size of the book could conveniently be increased without any interference with its format, this problem did not arise, but since the Seventeenth Edition it has been necessary to restrict any increase in the number of pages if it was to remain a "pocket book." With the rapid and continuous advances of medical science during recent years, and the ever-increasing volume of scientific literature, the problem has become more difficult of solution with each revision. Thus in spite of the drastic revision to which Volume I was subjected for the Twenty-first Edition, nearly sixty per cent. of the matter has been reset for this edition, and of this reset material by far the larger proportion is new to the book. It was clearly impossible to delete as obsolete or unimportant so large a part of a book which was thoroughly revised only four and a half years ago,

and the alternative of increasing the amount of matter in small type was adopted. Even so, the present volume is larger by over one hundred pages than its predecessor. In short, it would seem that the *Extra Pharmacopœia* is outgrowing its format and, with the conclusion of peace, the task of adequately presenting, within the existing limitations of space, the outpouring of medical research which will follow the renaissance of Europe, may become an insoluble problem. Nevertheless, to make any revolutionary change in the style and general appearance of a book which in its present form has served two generations of users is not a step to be undertaken lightly, and is one on which the views of readers would be welcomed.

### *Classification*

The classification, as in previous editions, is based upon the selection of parent substances in common use which serve to form sections of the book, thus enabling readers to review a group of medicinal agents of related composition or medicinal action with the minimum amount of inconvenience. These principal or parent substances are arranged alphabetically, and in each section are included those compounds which are chemically related and those substances which, although not having a close connection by constitution or origin, bear a somewhat similar pharmacological action or are frequently used for the treatment of the same ailment or disease. For example, the several official barbiturates are grouped under the heading "*Barbitonum*," and in this section will be found all the information concerning the many well-known proprietary and non-proprietary barbiturates, together with closely related substances, their more complex derivatives, and the compounded preparations which depend for their action wholly or partly upon the presence of one of these hypnotics. Similarly, under the heading "*Arsenum*," there is a systematic presentation of the information which is necessary to understand the composition, properties and application of the simple inorganic arsenic compounds, and the complex organic arsenicals such as Tryparsamide and Neoarsphenamine.

A few minor changes within this general framework\* are worthy of note. Thus, certain of the vitamins, after prolonged experimental and clinical research, have now passed into current therapeutic use, so that their continued inclusion in such arbitrary sections as *Aurantium* and *Cerevisiae Fermentum* is no longer justified, especially in the case of those vitamins now prepared synthetically. Ascorbic Acid, Aneurine Hydrochloride and Calciferol have therefore been raised to the status of principal substances and will be found in their respective alphabetical positions in the book. Curiously enough, the first of the vitamins to be discovered, vitamin A, has not yet emerged from the "vitamin" stage, possibly owing to the fact that its therapeutic indications are not yet sufficiently clear-cut, and this therefore remains as a subsidiary substance under *Oleum Morrhuae*.

As in previous editions, the sex hormones have been incorporated in one section, but the generic name *Œstrinum* has been dropped in favour of the more specific name *Œstradiol*. In due course, from the multiplicity of substances described under this heading, there will probably emerge one or two of proved therapeutic superiority, and the introduction of synthetics such as Stilbœstrol, Hexœstrol and Testosterone Propionate will serve to accelerate the process of elimination. Pending such a crystallisation it has been felt preferable to retain all these substances under one heading. The numerous active principles of the pituitary have been dealt with on the same principle.

### *New Pharmacopœias and Formularies*

Originally it was intended to publish this volume of the *Extra Pharmacopœia* after the issue of revised editions of the *British Pharmacopœia* and *British Pharmaceutical Codex*, both of which were due to appear in 1941. The war has, however, caused the Pharmacopœia Commission and Codex Revision Committee to postpone the issue of new editions and to issue, at frequent intervals, Addenda and Supplements to the *B.P.* 1932 and *B.P.C.* 1934 respectively. At the time of going to press two such Addenda (*B.P. Add. II* and *III*) to the *Pharmacopœia* have appeared, and one Codex Supplement, on Standard Dressings, has been published. The matter contained in these books has been incorporated in this edition. In addition, a fourth *B.P. Addendum* and a second Codex Supplement are in course of preparation, and although the work on this volume was too far advanced to await their appearance, it will probably be found that, so far as new substances are concerned, most of the essential information, with the exception of that relating to standards, is already included in our pages. There are also included notes of the more important recommendations taken from the reports of the various Committees of the Pharmacopœia Commission published in 1939, and which have not yet been incorporated in an Addendum.

Two foreign pharmacopœias have been completely revised, the *French Pharmacopœia*, published in 1938, and the *Japanese Pharmacopœia*, in 1935. In addition, two supplements to the *United States Pharmacopœia XI*, and a second supplement to the *Netherlands Pharmacopœia V*, have been issued. All of these have been examined and the references in the *Extra Pharmacopœia* revised so as to bring it into line with the new volumes.

The *National Formulary for N.H.I. Purposes* reached its third edition in 1939, and now forms the basis of the *Drug Tariff Formulary* included in Part VII of the *Drug Tariff*. The preparations from this formulary included in the present edition have been brought up-to-date and a number of new ones added. Other additions include formulæ from the pharmacopœias of the principal London and provincial hospitals, and from the *Pharmacopœia for Use in Military Hospitals*, 1940.



### *Drugs in War-time*

As the war progresses, the need for strict economy in the use of drugs increases. Sources of a number of crude drugs, and of the raw materials for the manufacture of synthetics, are now closed to this country, and this, together with the necessity of conserving foreign exchange and avoiding the waste of shipping space by the importation of non-essential drugs and chemicals, renders the problem of finding adequate alternatives pressing. The Therapeutic Requirements Committee, appointed in September 1939 by the Medical Research Council, in consultation with the Ministry of Health, has submitted our drug requirements to an exhaustive examination, and their report on "*Economy in the Use of Drugs in War-time*" (M.R.C. War Memo., No. 3, H.M.S.O., 1941) provides much of the information necessary for dealing with this problem.

The next step is the authorisation of the use of recommended alternatives. The British Pharmacopœia Commission, by publishing the two war-time addenda (*B.P. Add. II* and *III*) and a number of notices in the *Gazettes*, has already gone a considerable way in this direction. *B.P. Add. II* provides a number of vitamin preparations to supplement the supply of cod-liver oil, permits the use of a number of fixed oils in place of olive oil in some official preparations, and provides alternative formulæ for two ointments previously made with lard. *B.P. Add. III* contains similar alterations and amendments and also modifies the standard for ipecacuanha in order to extend the range of official varieties of this drug (*see p. 655*). More recently a notice in the *Gazettes* has authorised, among other items, the use of Indian squill and Indian valerian in place of squill and valerian, and of a solution of sodium lactate in place of glycerin in kaolin poultice. The fourth Addendum to the Pharmacopœia and the second Codex Supplement, when published, will increase still further the range of permissible alternatives and the number of modified formulæ for *B.P.* and *B.P.C.* preparations containing drugs in short supply. Nevertheless, the authority of the Pharmacopœia Commission and of the Codex Revision Committee is limited to the drugs and preparations contained in their respective publications. Wider authority must come from the Government, which, by means of orders issued under a Defence Regulation, can exercise whatever control is desirable. One such order, relating to the substitution of certain potassium salts by the corresponding sodium salt has already been published (*see p. 1151*). Further similar orders are to be expected and will furnish official guidance as to which drugs should not be used, or should be used sparingly, and what are the more plentiful substitutes. All the alterations, amendments or substitutions, which had been authorised up to the time of going to press, are incorporated in this book, and we stress the desirability in the national interest, that whenever and wherever possible, the alternatives should be used.

### ***Proprietary Names***

The inclusion of details concerning proprietary medicines has always been an important feature of the *Extra Pharmacopœia*, which is practically the only concise and comprehensive source of information of this type available. In the majority of cases the notes as to composition, dosage and uses are taken from the literature issued by the manufacturers or agents, upon whom rests the responsibility for the correctness of these statements. Every effort is made to keep the information upon proprietary medicines up-to-date by the deletion of articles no longer on the market and the inclusion of new ones, so that the user of the book is provided with information on nearly every branded product available to medicine and pharmacy.

An innovation made during the course of the last revision of Volume I was the inclusion in brackets, following the name of a proprietary article, of the name of the manufacturer and/or agent, and of his town. This system, which was experimentally tried in an appendix to the *B.P.C.* 1934 has proved to be of great value. Unfortunately, while there are few difficulties in the way of presenting such information in peace time, it is a very different matter under war-time conditions, especially when dealing with foreign medicines. At first sight, it seemed that it would be necessary to omit them. Further consideration, however, suggested that readers would thereby be deprived of the convenience of comparing the composition and uses of a foreign proprietary which they had been using, or had been recommended to use, with those of a suggested British alternative. Further, in the case of a foreign proprietary of complex chemical composition, they might easily have difficulty in tracing the British equivalent disguised under a different trade name. There was the further point that the agents for a foreign manufacturer in this country might still hold stocks of certain of that firm's proprietaries. As a compromise, therefore, it was decided to delete the less well-known proprietaries of continental origin, or those of minor importance, and to retain the remainder, together with the names of the manufacturers and agents, as before. Readers are therefore asked to bear in mind that the inclusion of a foreign proprietary is not an indication that it is obtainable in this country. The information is included merely for reference purposes, and for details as to the availability of the preparation recourse must be had to the agent.

A further complication, from the prescriber's point of view, arises as a result of the licences granted by the Comptroller of Patents to certain British firms to manufacture and market a number of important synthetic proprietaries previously obtained from abroad. A number of these, though described under official names in the *B.P. Addenda*, are also available under various trade names coined by the British manufacturers, and, in addition, under the original trade name of the foreign proprietary which is still on the market in this country, being either manufactured here by a

British-owned company or imported from America. A doctor who has been used in the past to prescribing a well-known foreign proprietary and who has difficulty in connecting it immediately with the official name or with one of the British equivalents, will find the present volume a useful aid to memory. It is unfortunate that in many instances new trade names should have been coined for these substances, thus adding to the confusion. Those firms which have marketed their products under the official titles are at a disadvantage in our pages, since it is impossible to give the names of manufacturers of pharmacopœial substances except when they are issued under trade names.

Finally, there are some instances in which the proprietary medicine is no longer available under its original foreign trade name in this country but is now manufactured by a British firm under another name. In these cases, in order to help the reader, we have followed the British trade name with the note in brackets "A foreign proprietary of similar composition was formerly marketed in this country under the Registered Trade Name —."

### ***Poisons and Dangerous Drugs***

As in previous editions, the *Extra Pharmacopœia* provides the doctor and pharmacist with a complete guide to the application of the law relating to the sale and supply of poisonous substances. The system adopted in the Twenty-first Edition for this purpose has proved satisfactory in the readiness with which it enables the reader to ascertain the legal position of any substance, and it has been continued in the present edition. To-day poisons are in one of two parts of the Poisons List of the Pharmacy and Poisons Act, 1933, their position being further qualified by a number of schedules to the Poisons Rules, 1935, which determine the special restrictions, exemptions or other conditions which apply to the various groups.

At the beginning of each section containing a group of poisons, the corresponding item in the Poisons List is quoted and its position marked by [P1] for Part 1 or [P2] for Part 2. Similarly, items from the schedules appended to the Poisons Rules are given to indicate whether the sale or supply of substances in the group are subject to any special restrictions or exemptions. The least complicated system possible has been devised for this purpose, and readers should note that the symbols [S1] and [S4], for example, refer respectively to Schedules I and IV of the Rules. Dangerous drugs are indicated by the symbol [D]. Preceding the names of substances which are poisons, readers will observe symbols or groups of symbols, from which they obtain without effort a concise summary to the conditions which apply. Thus, [P1-S1] tells him that he is concerned with a Part I poison, subject to the special restrictions governing the poisons in Schedule I. Likewise, [P1-S1-S4] indicates that the substance is in Part I of the Poisons List, that it is included in Schedules I and IV and,

consequently, supplied to the public only by authorised sellers on the prescription of a doctor, dentist or veterinary surgeon.

### ***Some Important Therapeutic Agents Described***

The following notes give a brief indication of some of the many important substances dealt with and draw attention to a few of the new therapeutic agents described.

**Acidum Aceticum.** Carbachol and the allied substance, acetyl- $\beta$ -methylcholine chloride, both of which were briefly described in the Twenty-first Edition under proprietary names, are now more adequately dealt with under these non-proprietary designations (p. 13).

**Acidum Ascorbicum.** Owing to the importance which this vitamin has assumed during recent years and to its increasing employment as a therapeutic agent, it has been removed from its subsidiary position under *Aurantium* and is now given greater prominence as a principal substance. Under this heading are also described vitamin K, methylnaphthoquinone, and vitamin P (p. 21).

**Acidum Mandelicum.** The use of mandelic acid and its salts in the treatment of urinary affections may now be regarded as a procedure of established therapeutic value, and these substances have been made the subject of a separate monograph (p. 81).

**Acidum Salicylicum.** The various esters of *p*-hydroxybenzoic acid and their use as preservatives in cosmetics and pharmaceutical preparations are dealt with (p. 104).

**Acidum Tannicum.** Though regarded until quite recently as almost the ideal procedure for the treatment of burns, tannic acid is now shown to possess certain disadvantages, and its use is definitely condemned in burns of the hands and face. Various modifications of the original technique are described (p. 112).

**Adrenalinum.** The matter under this heading has been revised and details are given of compounds related to adrenaline recently introduced to medicine, including the new circulatory stimulant, pholedrine (p. 132).

A new section has been added under the heading "Suprarenal Cortical Hormones," in which are described corticosterone and desoxycorticosterone acetate. The use of the latter in Addison's disease and in shock is the subject of numerous abstracts (p. 142).

**Aneurinæ Hydrochloridum.** Here again, as with ascorbic acid, the increasing importance of this vitamin was felt to justify its incorporation as a main monograph. The information under this new heading has been entirely rewritten and greatly extended (p. 188).

As subsidiaries to this section, and new to Volume I, are riboflavin, pyridoxin and nicotinic acid. The use of the latter (and of its amide) in acute pellagra is described (p. 192).

**Antimonium.** The new *B.P.* substance *Stibophenum*, for use in the treatment of schistosomiasis, undulant fever and oriental sore, is adequately dealt with (p. 198).

**Arsenum.** The whole of this section, and particularly that dealing with organic arsenic compounds, has been extensively revised (p. 209).

Carbarsone, a valuable medicament in the treatment of chronic intestinal amœbiasis, is now manufactured in this country under various proprietary names (p. 221).

A new rapid treatment of syphilis, of which doubtless more will be heard, is the intravenous drip therapy, as described under neoarsphenamine and Mapharside (pp. 230 and 235).

**Azorubrum.** The use of gentian violet, either in the form of an aqueous solution or a jelly, is now widely advocated to replace tannic acid in the treatment of burns, especially as a first-aid procedure. In the form of a 2 per cent. solution this dye is also finding increasing use in the treatment of a wide variety of mycotic skin affections (p. 255).

**Barbitonum.** The new *B.P.* substances *Hexobarbitonum*, *Hexobarbitonum Solubile*, and *Pemitonum* (hitherto known only under proprietary names) are described, together with a number of other barbiturates which have appeared on the market since our last revision (p. 275).

Sodium diphenylhydantoinate, an anticonvulsant for use in the treatment of epilepsy, is also dealt with in this section (p. 284).

**Belladonna.** An adequate appreciation, including numerous abstracts, of the so-called "Bulgarian Cure" of post-encephalitic parkinsonism is given (p. 291).

**Bismuthum.** An interesting new anti-syphilitic introduced from America is sobisminol, which is claimed to be effective by the oral route. Abstracts from the American literature are appended (p. 305).

**Bromum.** The information on the basal narcotic now known as *Bromethol* has been entirely rewritten in order to bring it into line with the latest clinical reports (p. 316).

**Calciferol.** This has now been removed from its subsidiary position under *Oleum Morrhuæ* and forms the subject of a separate monograph, in which are included vitamin A and the numerous proprietary preparations containing the two vitamins A and D (p. 326).

**Camphora.** Among the important substances dealt with in this section are sodium, calcium, and magnesium camphor-sulphonate, leptazol, and nikethamide. The use of leptazol in schizophrenia is the subject of numerous abstracts (p. 346).

**Cerevisiæ Fermentum.** In the absence of any distinctive name and in view of its still uncertain therapeutic status, vitamin E is retained in this section, though the information has been revised and extended (p. 386).

Penicillin, a substance produced during the growth of certain moulds, is shown to possess an even greater bacteriostatic action than some of the sulphonamides, and its introduction to medicine promises to open up an interesting new field of research (p. 385).

**Chlorinum.** A British Standards Specification for Bleach Ointment, or Anti-gas Ointment No. 1, is given together with formulæ for other bleach ointments which have appeared in the pharmaceutical literature (p. 398).

In this connection it is of interest to note that, to the best of our knowledge, the late W. H. Martindale was the first to advocate the use of an ointment of chlorinated lime in the treatment of mustard gas burns (see Preface to the *Extra Pharmacopœia*, Seventeenth Edition, Vol. I, 1922).

**Chloroformum.** Under "Anæsthetic Hydrocarbons" the information on cyclopropane and vinyl ether has been revised. The advantages and limitations of these two anæsthetics are now more clearly appreciated (p. 407).

**Chrysarobinum.** The properties and uses of dithranol are described. This substance which was previously only available as a foreign proprietary is now manufactured in this country (p. 412).

**Cresol.** Two new sections have been included in this monograph under the headings "Chloro-phenolic Antiseptics" and "Higher Phenolic Antiseptics"; among others, chlorocresol, parachlorometaxilenol, parachlorophenol and amylmetacresol are described, and a number of abstracts from the scientific literature are appended, together with details of proprietary preparations containing these antiseptics (p. 467).

**Ephedra.** A great deal of clinical research has been conducted on amphetamine sulphate during the past two or three years, and it has now assumed considerable therapeutic importance (p. 500).

**Gelatinum.** The small but hitherto separate sections on Capsulæ, Lamellæ and Pastillæ are now incorporated under this heading (p. 542).

A description of pectin and abstracts dealing with its employment as a hæmostatic and in infantile diarrhoea are included in this section. The use of apple powder in the latter condition also forms the subject of several abstracts (p. 544).

**Glycerinum.** During recent years the glycols have become increasingly used both in pharmaceutical and cosmetic preparations and for various industrial purposes. The glycols in common employment are described, with notes on their uses and their toxicities (p. 554).

**Hepar.** The information under this heading has been brought up to date, including the list of proprietary preparations containing liver, or the active principles of liver (p. 556). This list, which does not profess to be exhaustive, now contains details of no less than fifty-four proprietaries. The recent memorandum of the Food Rationing Advisory Committee of the Medical Research Council deprecating the use under present conditions of oral preparations of liver in pernicious anæmia, will probably serve to reduce this list considerably in the near future without causing any serious loss to medicine.

The anti-coagulant substance heparin, which is prepared from liver, is dealt with at some length (p. 575).

**Insulin.** This important monograph has again been carefully revised and a new section added on protamine insulin compounds (p. 634).

**Iodum.** The information concerning the use of iodised oils for diagnostic purposes has been transferred to this monograph from Volume II. The contrast media diodone and iodoxyl are also described (p. 650).

**Ligatures and Sutures.** This monograph has been entirely rewritten for this edition (p. 671).

**Oestradiol.** The rapid advances in knowledge both in respect of the chemistry and the physiology of the sex hormones, which have taken place since our last revision, together with the introduction of synthetic substances, have necessitated a complete rewriting of this section, which now occupies 26 pages as compared with 13 pages in the Twenty-first Edition (p. 714).

In an attempt to clarify the somewhat confusing position, from the therapeutic aspect, due to the availability of numerous oestrogenic substances all possessing similar actions, a short section has been incorporated in which the therapeutic activities of the various oestrogens are compared and, while each of the substances is separately described, their uses are dealt with in one comprehensive section. The androgens have been treated in a similar manner (p. 734).

Another matter which received careful consideration was the method of inclusion of the large number of proprietary preparations, especially in view of the differing methods of presentation and of dosage employed by manufacturers. A list of the proprietaries containing a particular oestrogen (or androgen) is appended at the end of the section dealing with that substance, and wherever possible the strength is given in international units.

Among the new substances described in this section are oestradiol benzoate, stilboestrol, stilboestrol dipropionate, hexoestrol, pregneninolone, and testosterone propionate.

**Paraffinum.** A new section has been added under the heading "Higher Fatty Alcohols." Cetyl alcohol, stearyl alcohol, and Lanette Wax SX are described (p. 787).

**Pituitarium.** The information concerning the posterior lobe has been extensively revised (p. 832), while that on the anterior lobe has been rewritten (p. 837). Since our previous revision an enormous amount of research work has been conducted on the active principles of the anterior lobe, as a result of which their functions and therapeutic indications have become more clearly defined, though many of them have not yet been isolated in a pure form. The one which has so far provided the most encouraging clinical results is the gonadotrophic principle, and this is dealt with at some length. The gonadotrophic hormone derived from the pituitary itself, and the gonadotrophic factors obtained from pregnancy urine and from pregnant mares' serum, are described under separate headings, as are the numerous proprietary preparations containing these respective factors (p. 840).

**Quinina.** The information on the anti-malarials *Pamaquina*, *Mepacrine Hydrochloridum*, and *Mepacrine Methanosulphonas*, all of which were previously described under trade names, has been revised and numerous abstracts added (p. 889).

**Sapones.** An interesting new section under this heading is that on "Sulphonated Fatty Alcohols." Triethanolamine and triethanolamine stearate, both of which are being increasingly used in pharmacy and in the cosmetic industry, are also described (p. 907).

**Sulphanilamidum.** That the importance of the sulphonamides has been sufficiently appreciated may be gauged from the fact that this new section occupies no less than 37 pages. It is, in fact, the largest section devoted to any single group of substances in the book (p. 936). It is doubtful whether in the whole history of medicine any therapeutic agent has given rise to such a vast outpouring of literature in such a brief period of time as the sulphonamides, and the task of abstracting only the more important of the thousands of papers which have appeared has been no light one. The collation of the enormous amount of material which finally accumulated, and its presentation in a manner which would cover every important aspect of the subject clearly and concisely, without "overloading," called for very careful consideration. Thus, there were in our files scores of abstracts dealing solely with the toxic effects of sulphanilamide. More than half of these were discarded as merely repetitive, but there still remained a very large number. Instead therefore of adopting the usual method of putting all these abstracts together in chronological order, it was thought better to group them under the heading of the particular toxic effect to which they referred.

The difficulty presented itself in an even more acute form in the preparation of the Uses sections of sulphanilamide and sulphapyridine. It was felt that to attempt to incorporate detailed information on the treatment of the wide variety of diseases for which these substances are used in a general statement, and to follow this in each case with ten or twelve pages of abstracts in unbroken sequence would have been a clumsy and unsatisfactory procedure. It was therefore decided to make only a short general statement and to preface each group of abstracts dealing with the more important indications with a brief summary giving the dosage, method of treatment, etc., applicable to the particular disease. This arrangement it is hoped will make for ease of reference.

The main substances dealt with in this section are sulphanilamide, sulphapyridine and sulphathiazole, and in addition details are given of the numerous sulphonamide derivatives issued under proprietary names. There is more than a likelihood that even more potent and valuable chemotherapeutic agents of the sulphonamide series will be introduced to medicine in the very near future which may supersede those at present employed. Be that as it may, it was felt that this should not deter us from presenting the most adequate



account possible to date of what promises to be one of the most important advances ever made in the treatment of disease.

### ***Vaccines, Sera, Toxins and Antitoxins***

The striking advances in the realm of chemotherapy during recent years have to some extent overshadowed the numerous but less spectacular achievements recorded in bacteriotherapy, especially as, by a strange coincidence, the sulphonamides have registered their most outstanding successes in just those diseases in which vaccine and serum therapy have but recently established their value beyond cavil, *e.g.*, pneumonia, cerebrospinal fever and gas gangrene. Nevertheless, that much important work has been done since our last edition is evidenced by the fact that some fifty per cent. of this section of the book has been entirely rewritten and the remainder substantially revised, and that the completed section is 11 pages longer than its predecessor. Among the diseases under which the matter has been rewritten may be mentioned Gas Gangrene, Influenza, Measles, Pneumonia, Rheumatoid Arthritis, Scarlet Fever, Tetanus, and Whooping Cough. Other items of interest which are new to the book, or which have been extensively revised, include the following:

*Oral Cold Vaccines*—a discussion as to their prophylactic value, together with details of a number of proprietary vaccines.

*Diphtheria*—an evaluation of the various diphtheria prophylactics and a précis of the instructions issued by the Ministry of Health re Immunisation against Diphtheria, and a description of the Tellurite Test for diagnosis, together with criticisms of the test.

*Snake Venoms*—the dosage and therapeutic uses in respect of Cobra Venom, Puff-adder Venom, Moccasin Venom and Viper Venom, with numerous abstracts from the medical literature.

*Tuberculosis*—a description of Tuberculin P.P.D. and of the Vollmer and Copenhagen Patch Tests.

*Typhoid*—an evaluation of Anti-Typhoid Serum (Felix).

*Variola*—the present situation in respect of post-vaccinal encephalitis and references to Chick Embryo Vaccine Lymph.

### ***Blood Transfusion***

The emergence of blood transfusion from the status of a hazardous procedure, only to be undertaken in rare emergencies by a specialist, to that of a safe and comparatively simple measure employed as a routine even under field conditions, is one of the major therapeutic advances of permanent value which may be almost directly attributed to the exigencies of the war. The various steps which have made possible the more widespread use of this life-saving measure—first the introduction of stored blood, then of citrated plasma, and finally of dried plasma and serum—are described in our pages. Although the transfusion of plasma or serum has now largely superseded whole blood transfusion, especially in the treatment of shock, the latter is still indicated in certain conditions, *e.g.*, in severe anæmia, and the systems of

classification of the blood groups are given, together with the technique of blood grouping and the method of collection of blood from the donor. The technique of transfusion into the patient (applicable to all the solutions), whether by means of single transfusion or continuous drip transfusion, is outlined, and the possible reactions described. Throughout the section (pp. 1096-1105) the most recent recommendations issued by the authorities are incorporated, together with numerous abstracts from the literature.

### ***Summaries of Legal Requirements***

The section on Poisons towards the end of the book contains the practical summary of the Poisons Rules, 1935, which was first included in the Twentieth Edition, revised and amended in the light of the Poisons (Amendment) Rules, 1937, 1938 and 1940. It provides the reader with a concise account of the conditions governing the sale or supply of poisons by the doctor, dentist or veterinary surgeon, the pharmacist, the wholesaler and the hospital. This is followed by the Poisons List and the Schedules to the Poisons Rules, brought up-to-date by the inclusion of the alterations made by the Poisons List (Amendment) Orders, 1937, 1938 and 1940, and by the Poisons (Amendment) Rules, 1937, 1938 and 1940 respectively, and these in turn are followed by the Poisons Schedule applicable to Northern Ireland and to Eire, both likewise corrected to 1940. The second part of this section contains a summary of the Dangerous Drugs legislation, including all the recent changes and an outline of the principal points to be remembered by the prescriber and dispenser, together with a summarised version of the Therapeutic Substances Act and Rules, as amended by Statutory Rules and Orders issued in 1935, 1937 and 1939. This section is concluded by the inclusion of a summary of the Shortage of Drugs Order authorising the substitution of a number of potassium salts by the corresponding sodium salt when the former are prescribed or demanded.

### ***Therapeutic Index***

During the course of revision it was decided that the usefulness of this Index might be considerably enhanced if each entry relative to a medicinal substance were followed by its appropriate page number in the body of the book, thus making the section self-contained. This necessitated the compiling of an entirely new Therapeutic Index. The text was therefore systematically perused, starting from page 1 and continuing to the end, and an entry made in respect of every reference to the use of a drug or chemical in a particular disease. Proceeding along these lines it became obvious that the existing alphabetical arrangement of drugs and chemicals in each paragraph might conveniently be replaced by a page arrangement, commencing with the lowest page and progressing systematically to the highest. Thus, the physician when confronted with a case which has proved resistant to those therapeutic

measures which he has instituted, is now able by reference to the Therapeutic Index to run quickly through all the medicinal substances mentioned throughout the book in connection with the treatment of the ailment which he has under consideration, without having to refer back to the main index or to dodge backwards and forwards over the pages of the text.

It should be understood that this index does not claim to present an exhaustive list under each disease of the drugs and chemicals employed in its treatment. It contains no entries in respect of therapeutic agents which are not referred to, either specifically or by inference, in the text as having been employed in the treatment of a particular disease, since it was felt that to refer the reader to a page which contained no mention of a therapeutic indication would cause more annoyance than if the reference to the use of the drug in that disease were omitted altogether. However, since the Uses sections throughout the book have been thoroughly revised in the light of the most recent knowledge, and the abstracts are as comprehensive and up to date as it is possible to make them, it is unlikely that the omissions will be found to include many therapeutic agents of major importance.

### ***Acknowledgments***

Throughout the revision the fullest use has been made of medical and pharmaceutical literature, and as far as possible care has been taken to select matter which is likely to be of most value to the physician and the pharmacist. In reviewing such a wide range of pharmacopœias, formularies and literature, it is probable that some points of importance may have been overlooked, or that typographical errors may have occurred. The Editor and the Revision Committee will be grateful if readers will draw their attention to any such errors, and they will welcome suggestions regarding the subject matter or arrangement of the work from physicians or pharmacists.

During the latter period of the revision the Committee were deprived by illness of the services of the Editor, and his personal responsibility for the contents is consequently less complete than in previous editions. The Committee desire to record their appreciation of the services of Mr. S. Ward, who assumed the responsibility under their direction for completing the revision. He successfully discharged a formidable task with energy and ability.

*London, May 1941.*

# ABBREVIATIONS

The abbreviated titles of journals are those given in the *World List of Scientific Periodicals* (2nd Edn., 1934). When the reference is to a periodical of which two volumes are published during a year the number placed first indicates the first or second volume of the year followed by the year, and the last number refers to the page, thus, *Brit. med. J.*, i/1932, 250. When only one volume of a periodical is published each year, the reference gives the year and the page, thus, *Quart. J. Pharm.*, 1934, 341. In other cases the volume number is given in italics in addition to the year and page, thus, *J. biol. Chem.*, 1928, 77, 787.

$\alpha$ —optical rotation.

A.O.A.C.—Methods of Analysis of the Association of Official Agricultural Chemists, Washington.

A.P.F.—Australian Pharmaceutical Formulary.

A.R.—Reagent for Analytical Purposes.

*Acta paediatr.*, *Stockh.*—*Acta paediatrica*.

Allen—Allen's Commercial Organic Analysis. 5th Edn., Vols. I-VI edited by S. S. Sadler, E. C. Lathrop and C. A. Mitchell; Vols. VII-X edited by C. A. Mitchell (1924-1933).

*Amer. J. Cancer*—American Journal of Cancer.

*Amer. J. Dis. Child.*—American Journal of Diseases of Children.

*Amer. J. Hyg.*—American Journal of Hygiene.

*Amer. J. med. Sci.*—American Journal of Medical Sciences.

*Amer. J. Obstet. Gynec.*—American Journal of Obstetrics and Gynecology.

*Amer. J. Pharm.*—American Journal of Pharmacy.

*Amer. J. Physiol.*—American Journal of Physiology.

*Amer. J. Publ. Hlth.*—American Journal of Public Health.

*Amer. J. Syph.*—American Journal of Syphilis.

*Amer. J. trop. Med.*—American Journal of Tropical Medicine.

*Amer. Perfum.*—American Perfumer and Essential Oil Review.

*Amer. Rev. Tuberc. (Suppl.)*—American Review of Tuberculosis (Supplement).

*Analyst*—Analyst.

*Ann. Eugen.*, *Camb.*—Annals of Eugenics.

*Ann. Falsif.*—Annales des Falsifications.

*Ann. Hyg. publ.*, *Paris*—Annales d'hygiène publique et de médecine légale (industrielle et sociale).

*Ann. Inst. Pasteur*—Annales de l'Institut Pasteur.

*Ann. Surg.*—Annals of Surgery.

*Ann. trop. Med. Parasit.*—Annals of Tropical Medicine and Parasitology.

*Apothekerztg.*, *Berl.*—Apothekerzeitung, Berlin.

*Arch. Derm. Syph.*, *N.Y.*—Archives of Dermatology and Syphilology.

*Arch. Dis. Childh.*—Archives of Disease in Childhood.

*Arch. exp. Path. Pharmak.*—Archiv für experimentelle Pathologie u. Pharmakologie.

*Arch. int. Pharmacodyn.*—Archives internationales de pharmacodynamie et de thérapie.

*Arch. intern. Med.*—Archives of Internal Medicine.

*Arch. Kinderheilk.*—Archiv für Kinderheilkunde.

*Arch. klin. Chir.*—Archiv für klinische Chirurgie.

*Arch. Méd. Enf.*—Archives de médecine des enfants.

*Arch. Pharm.*, *Berl.*—Archiv der Pharmazie.

*Arch. Pharm. Chemi.*—Archiv für Pharmaci og Chemi.

*Arch. Neurol. Psychiat.*, *Lond.*—Archives of Neurology and Psychiatry.

*Arch. Radiol. Electrother.*—Archives of Radiology and Electrotherapy.

*Ass. méd.*—Association médicale.

*Aust. J. Pharm.*—Australian Journal of Pharmacy.

B.H.P.—British Homeopathic Pharmacopœia.

b.p.—boiling-point.

B.P.—British Pharmacopœia, 1932.

B.P. Add. I, II and III.—First (1936), Second (1940) and Third (1941) Addenda to the British Pharmacopœia, 1932.

B.P.C.—British Pharmaceutical Codex, 1934.

B.P.C. Supp.—Standard Dressings Supplement (1940) to the B.P.C.

- B.V.H.*—Bristol Voluntary Hospitals Pharmacopœia, 1935.  
*Ber. dtsch. chem. Ges.*—Bericht der Deutschen Chemischen Gesellschaft.  
*Berl. klin. Wschr.*—Berliner klinische Wochenschrift.  
*Biochem. J.*—Biochemical Journal.  
*Biochem. Z.*—Biochemische Zeitschrift.  
*Boll. Ist. sieroter., Milano*—Bollettino dell'Istituto sieroterapico milanese.  
*Brit. chem. Abstr.*—British Chemical Abstracts. (A) Pure Chemistry. (B) Applied Chemistry.  
*Brit. colon. Drugg.*—British and Colonial Druggist (since 1915—British and Colonial Pharmacist).  
*Brit. colon. Pharm.*—British and Colonial Pharmacist.  
*Brit. dent. J.*—British Dental Journal.  
*Brit. J. Actino-Therap.*—British Journal of Actinotherapy and Physiotherapy.  
*Brit. J. Biophys.*—British Journal of Biophysics.  
*Brit. J. Child. Dis.*—British Journal of Children's Diseases.  
*Brit. J. Derm.*—British Journal of Dermatology.  
*Brit. J. exp. Path.*—British Journal of Experimental Pathology.  
*Brit. J. phys. Med.*—British Journal of Physical Medicine.  
*Brit. J. Radiol. (B.A.R.P. Sect.)*—British Journal of Radiology (British Association for the Advancement of Radiology and Physiotherapy Section), continued since 1927 as British Journal of Radiology, New Series.  
*Brit. J. Radiol., N.S.*—British Journal of Radiology, New Series.  
*Brit. J. Radiol. (Röntg. Soc. Sect.)*—British Journal of Radiology (Röntgen Society Section), continued since 1927 as British Journal of Radiology, New Series.  
*Brit. J. Surg.*—British Journal of Surgery.  
*Brit. J. vener. Dis.*—British Journal of Venereal Diseases.  
*Brit. med. J.*—British Medical Journal.  
*Brit. med. J. Epit.*—British Medical Journal Epitome.  
*Brompton H.*—Pharmacopœia of the Hospital for Consumption and Diseases of the Chest, 11th Edn., 1928.  
*Brooke*—Tropical Medicine, Hygiene and Parasitology, by Gilbert E. Brooke, 1920.  
*Bruce and Dilling*—Bruce and Dilling's Materia Medica and Therapeutics, by W. J. Dilling, 14th Edn., 1933.  
*Bull. Acad. Méd., Paris*—Bulletin de l'Académie de médecine.  
*Bull. Dep. Agric. Can.*—Bulletin of the Department of Agriculture of the Dominion of Canada.  
*Bull. Féd. int. Pharm.*—Bulletin de la Fédération internationale pharmaceutique.  
*Bull. Hlth Org. L. o. N.*—Bulletin of the Health Organisation of the League of Nations.  
*Bull. Hyg.*—Bulletin of Hygiene.  
*Bull. imp. Inst., Lond.*—Bulletin of the Imperial Institute.  
*Bull. Inst. Pasteur*—Bulletin de l'Institut Pasteur.  
*Bull. med., Paris*—Bulletin medical, Paris.  
*Bull. Off. int. Hyg. publ.*—Bulletin mensuel de l'Office internationale d'hygiène publique.  
*Bull. Sci. Pharm.*—Bulletin des Sciences pharmacologiques.  
*Bull. Soc. chim. Fr.*—Bulletin, Société chimique de France.  
*Bull. Soc. méd. Hôp. Paris*—Bulletin et mémoires de la Société médicale des hôpitaux de Paris.  
*Bull. tech. Mus., Sydney*—Bulletin of the Technological Museum, Sydney.  
*C.H.W.*—Formulæ of Chelsea Hospital for Women, 1927.  
*C.I.S.*—Commission Internationale des Spécialités.  
*C.L.T.H.*—Formulæ of the Central London Throat, Nose and Ear Hospital, 3rd Edn., 1924.  
*C.X.H.*—Charing Cross Hospital Pharmacopœia, 1935.  
*Canad. Form.*—The Canadian Formulary, 1933.  
*Canad. med. Ass. J.*—Canadian Medical Association Journal.  
*Canad. publ. Hlth J.*—Canadian Public Health Journal.  
*Chem. Abstr.*—Chemical Abstracts.  
*Chem. & Drugg.*—Chemist and Druggist.  
*Chem. & Ind.*—Chemistry and Industry, of the Society of Chemical Industry.  
*Chem. Ind. Rev.*—Chemistry and Industry Review.  
*Chem. Weekbl.*—Chemische Weekblad.

- Chem. Z.*—Chemische Zeitschrift.  
*Chem. Ztg.*—Chemische Zeitung.  
*Chininum*—Chininum Scriptiones Collectae, Bureau for increasing the use of Quinine, Amsterdam, 1925.  
*Clin. J.*—Clinical Journal.  
*cm.*—centimetre.  
*Colyer*—Colyer's Dental Surgery and Pathology, by Sir J. F. Colyer, 6th Edn., 1931, and earlier issues (previously Smale and Colyer's Diseases and Injuries of Teeth).  
*C.R. Acad. Sci., Paris*—Compte rendu hebdomadaire des séances de l'Académie des sciences.  
*C.R. Soc. Biol., Paris*—Compte rendu hebdomadaire des séances et mémoires de la Société de biologie.  
*Cushny*—Text-book of Pharmacology and Therapeutics, by A. R. Cushny, 10th Edn., revised by C. W. Edmunds and J. A. Gunn (1934).  
**[D]**—Drugs or preparations coming within the scope of the Dangerous Drugs Acts, 1920 (as amended) and not exempt from control under the Dangerous Drugs Regulations, 1937.  
*Dansk Tidsskr. Farm.*—Dansk Tidsskrift for Farmaci.  
*Dtsch. med. Wschr.*—Deutsche medizinische Wochenschrift.  
*Disp.*—Art of Dispensing, published by *The Chemist and Druggist*, London, 10th Edn., 1926.  
*Dixon*—Manual of Pharmacology, by the late W. E. Dixon, F.R.S., 7th Edn., 1929.  
*D.T.F.*—Drug Tariff Formulary, issued by the Ministry of Health.  
*E.G.A.*—Pharmacopœia of the Elizabeth Garrett-Anderson Hospital, 1926.  
*Ec. Prod. India*—Economic Products of India.  
*Edinb. med. J.*—Edinburgh Medical Journal.  
*Emery*—Clinical Bacteriology and Hæmatology, by W. d'Este Emery, 6th Ed., 1921.  
*Endocrinology*—Endocrinology.  
*F.E. VIII*—Farmacopea Española. Octava Edición, 1930.  
*f.p.*—freezing-point.  
*Fr. Cx.*—Codex Medicamentarius Gallicus, Pharmacopée Française (1937).  
*Finnemore*—Essential Oils, their Chemistry and Technology, by H. Finnemore, 1926.  
*g.*—gramme.  
*G.H.*—Pharmacopœia of Guy's Hospital, 1937.  
*Gehe*—Gehe's Codex, 6th Edn., 1933.  
*Ghosh*—Treatise on Materia Medica and Therapeutics, by the late R. Ghosh, I.M.S. Edited by B. H. Deane, 12th Edn., 1930.  
*Glasg. med. J.*—Glasgow Medical Journal.  
*gr.*—grain.  
*Gradwohl and Blaivas*—The Newer Methods of Blood and Urine Chemistry by R. B. H. Gradwohl and A. J. Blaivas, 2nd Edn., 1920.  
*Gt. Orm. H.*—Pharmacopœia of the Hospital for Sick Children, Great Ormond Street, 1933.  
*Hager*—Handbuch der Pharmaceutischen Praxis, revised by G. Fredericks, G. Arends and H. Zörnig, 1925.  
*Hale-White*—Hale-White's Materia Medica, Pharmacy, Pharmacology and Therapeutics, revised by A. H. Douthwaite, 24th Edn., 1939.  
*Hare*—Text-Book of Practical Therapeutics, by H. A. Hare, 21st Edn., 1930.  
*Harper Adams Util. Poul.*—Harper Adams Utility Poultry Journal.  
*Helv. chim. Acta*—Helvetica chimica acta.  
*Hewlett and McIntosh*—A Manual of Bacteriology, 9th Edn., revised by R. T. Hewlett and J. McIntosh, 1932.  
*Hoppe-Seyl. Z.*—Hoppe-Seyler's Zeitschrift für physiologische Chemie.  
*Hospitalstidende*—Hospitalstidende.  
*Hutchison*—Food and Principles of Dietetics, by R. Hutchison and V. H. Mottram, 7th Edn., 1933.  
*I.A.*—International Agreement, 1930.  
*I.H.*—Pharmacopœia of the Infants Hospital, Vincent Square, London, 1939.

*I.V.*—iodine value.

*I. c. Add.*—Indian and Colonial Addendum (1900) to the B.P. 1898.

*Indian J. med. Res.*—Indian Journal of Medical Research.

*Indian med. Gaz.*—Indian Medical Gazette.

*Indian med. Res. Mem.*—Indian Medical Research Memoirs.

*Industr. Engng Chem. (anal. Edn.)*—Industrial and Engineering Chemistry, (Analytical Edition).

*Int. Conf. trop. Amer.*—Proceedings of the International Conference on Health Problems in Tropical America, 1924, United Fruit Co., Boston.

*Int. J. Leprosy*—International Journal of Leprosy.

*Int. J. Med.*—International Journal of Medicine and Surgery, now included in *Surgical Journal*.

*J. R. Army med. Cps*—Journal of the Royal Army Medical Corps.

*J. R. nav. med. Serv.*—Journal of the Royal Naval Medical Service.

*J. agric. Sci.*—Journal of Agricultural Science.

*J. Allergy*—Journal of Allergy.

*J. Amer. chem. Soc.*—Journal of the American Chemical Society.

*J. Amer. diet. Ass.*—Journal of the American Dietetic Association.

*J. Amer. med. Ass.*—Journal of the American Medical Association.

*J. Amer. pharm. Ass., pharm. Abstr.*—Pharmaceutical abstracts published in the Journal of the American Pharmaceutical Association.

*J. Amer. pharm. Ass., pract. Pharm. Edn.*—Journal of the American Pharmaceutical Association, Practical Pharmacy Edition.

*J. Amer. pharm. Ass., Sci. Edn.*—Journal of the American Pharmaceutical Association, Scientific Edition.

*J. Ass. off. agric. Chem., Wash.*—Journal of the Association of Official Agricultural Chemists.

*J. biol. Chem.*—Journal of Biological Chemistry.

*J. Cancer Res.*—Journal of Cancer Research.

*J. chem. Soc.*—Journal of the Chemical Society.

*J. chem. Soc. Abstr.*—Journal of the Chemical Society Abstracts (continued since 1926 as British Chemical Abstracts).

*J. clin. Invest.*—Journal of Clinical Investigation.

*J. clin. Res.*—Journal of Clinical Research.

*J. comp. Path.*—Journal of Comparative Pathology and Therapeutics.

*J. Dairy Res.*—Journal of Dairy Research.

*J. Dairy Sci.*—Journal of Dairy Science.

*J. exp. Med.*—Journal of Experimental Medicine.

*J. Franklin Inst.*—Journal of the Franklin Institute.

*J. gen. Physiol.*—Journal of General Physiology.

*J. Hyg., Camb.*—Journal of Hygiene.

*J. Immunol.*—Journal of Immunology.

*J. Indian med. Ass.*—Journal of the Indian Medical Association.

*J. infect. Dis.*—Journal of Infectious Diseases.

*J. Instn elect. Engrs*—Journal of the Institution of Electrical Engineers.

*J. Lab. clin. Med.*—Journal of Laboratory and Clinical Medicine.

*J. Laryng.*—Journal of Laryngology (Rhinology) and Otology.

*J. ment. Sci.*—Journal of Mental Science.

*J. Obstet. Gynaec.*—Journal of Obstetrics and Gynaecology of the British Empire.

*J. Path. Bact.*—Journal of Pathology and Bacteriology.

*J. Pediat.*—Journal of Pediatrics.

*J. Pharm. Chim., Paris*—Journal de pharmacie et de chimie.

*J. Pharmacol.*—Journal of Pharmacology and Experimental Therapeutics.

*J. Physiol.*—Journal of Physiology.

*J. Prat., Paris*—Journal des praticiens.

*J. Röntgen Soc.*—Journal of the Röntgen Society, continued from 1924 to 1927 as The British Journal of Radiology (Röntgen Society Section), and since 1927 as The British Journal of Radiology, New Series.

*J. State Med.*—Journal of State Medicine.

*J. Soc. chem. Ind., Lond.*—Journal of the Society of Chemical Industry.

*J. Suisse Pharm.*—Journal suisse de pharmacie, now Schweizerische Apothekerzeitung.

*J. Text. Inst., Manchr.*—Journal of the Textile Institute, Manchester

*J. trop. Med. (Hyg.)*—Journal of Tropical Medicine and Hygiene.

- K.C.H.*—King's College Hospital Pharmacopœia, 1934.  
*Kenwood*—Public Health Laboratory Work, by H. R. Kenwood, 8th Edn., 1925.  
*Klin. Wschr.*—Klinische Wochenschrift.  
*Knox*—Radiography and Radio-Therapeutics, by Robert Knox, 4th Edn., in 2 vols. (Vol. II completed and edited by W. M. Levitt), 1923-32.  
*L.C.C.*—London County Council Pharmacopœia, 1936.  
*L.H.*—London Hospital Pharmacopœia, 1934.  
*L.L.*—London Lock Hospitals Pharmacopœia.  
*L.S.H.*—London Skin Hospital.  
*Lancet*—Lancet.  
*Leprosy Rev.*—Leprosy Review.  
*m.*—minim.  
*m.a.*—milliampere.  
*m.p.*—melting-point.  
*M.R.C.*—Medical Research Council.  
*M.R.I.*—Manchester Royal Infirmary Pharmacopœia, 1933.  
*May*—Chemistry of Synthetic Drugs, by Percy May, 3rd Edn., 1921.  
*Med. Annu.*—Medical Annual.  
*Med. J. Aust.*—Medical Journal of Australia.  
*Med. J. Rec.*—Medical Journal and Record.  
*Med. Klinik*—Medizinische Klinik.  
*Med. Offr.*—Medical Officer.  
*Med. Pr.*—The Medical Press and Circular.  
*Med. Rec., N.Y.*—Medical Record.  
*Medicine, Baltimore*—Medicine, Baltimore.  
*Mem. Univ. Calif.*—Memoirs of the University of California.  
*Merck*—E. Merck's Annual Report of recent advances in Pharmaceutical Chemistry and Therapeutics.  
*Merck's Index*—Merck's Index, 5th Edn., 1940.  
*Mfg Chem.*—Manufacturing Chemist.  
*mg.*—milligramme.  
*Mid. H.*—Middlesex Hospital Pharmacopœia, 1933.  
*Mikrochemie.*—Mikrochemie.  
*Milit. Surg.*—Military Surgeon.  
*ml.*—millilitre.  
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*n.*—refractive index.  
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*N.H.*—Prescription Formulæ for Use in Naval Hospitals, 1930.  
*N.I.F.*—National Formulary for National Health Insurance Purposes, issued by the British Medical Association, 3rd Edn., 1939.  
*N.N.R.*—New and Non-official Remedies, 1940, issued by the American Medical Association.  
*Nature, Lond.*—Nature, London.  
*Naturwissenschaften*—Naturwissenschaften.  
*Nav. med. Bull., Wash.*—Naval Medical Bulletin, Washington.  
*New Engl. J. Med.*—New England Journal of Medicine.  
*Norsk farm. Tidsskr.*—Norsk farmaceutisk Tidsskrift.  
*Nutr. Abstr. Rev.*—Nutrition Abstracts and Reviews.  
*N.Y. St. J. Med.*—New York State Journal of Medicine.  
[P1]—Part 1 of the Poisons List.  
[P2]—Part 2 of the Poisons List.  
*P.E.H.C.*—Pharmacopœia of the Princess Elizabeth of York Hospital for Children (formerly the East London Hospital), 1933.  
*P.G. VI.*—German Pharmacopœia, 1926.  
*P.J.F.*—Pharmaceutical Journal Formulary.



- P.L.*—Pharmacopœia Londinensis, 1851.  
*P.M.C.E.*—Select Parliamentary Committee on Proprietary Medicines Enquiry, 1912-13.  
*P.M.H.*—Pharmacopœia for use in Military Hospitals (*H.M.S.O.*).  
*P. Argent. II*—Pharmacopœia of the Argentine Republic, 2nd Edn., 1919.  
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*P. Russ.*—Russian Pharmacopœia, 1934.  
*P. Svec.*—Swedish Pharmacopœia, 1925.  
*Paris méd.*—Paris médical. La semaine du clinicien.  
*Perfum. essent. Oil Rec.*—Perfumery and Essential Oil Record.  
*Ph. Form.*—Pharmaceutical Formulas, 9th Edn., Second Reprint, 1921, by Peter MacEwan; and 10th Edn., Vol. I, 1929, revised by S. W. Woolley and G. P. Forrester, Vol. II, 1934, revised by G. P. Forrester, *The Chemist and Druggist*, London.  
*Pharm. Acta Helvet.*—Pharmaceutica Acta Helvetiæ.  
*Pharm. J.*—Pharmaceutical Journal.  
*Pharm. Weekbl.*—Pharmaceutisch Weekblad voor Nederland.  
*Pharm. Zentralh.*—Pharmazeutische Zentralhalle f. Deutschland.  
*Pharm. Ztg. Berl.*—Pharmazeutische Zeitung.  
*Philipp. J. Sci.*—Philippine Journal of Science.  
*Physiol. Rev.*—Physiological Reviews.  
*Pr. méd.*—Presse médicale.  
*Practitioner*—Practitioner.  
*Prescriber*—Prescriber.  
*Proc. Mayo Clin.*—Proceedings of Staff Meetings of the Mayo Clinic.  
*Proc. nat. Acad. Sci.*—Proceedings of the National Academy of Science.  
*Proc. roy. Soc.*—Proceedings of the Royal Society.  
*Proc. roy. Soc. Edinb.*—Proceedings of the Royal Society of Edinburgh.  
*Proc. R. Soc. Med.*—Proceedings of the Royal Society of Medicine.  
*Proc. Soc. exp. Biol., N.Y.*—Proceedings of the Society for Experimental Biology and Medicine.  
*Publ. Hlth, Lond.*—Public Health.  
*Publ. Hlth Rep., Wash.*—Public Health Reports, issued by the United States Public Health Service.  
*Quart. Bull. Hlth Org. L. o. N.*—Quarterly Bulletin of the Health Organisation of the League of Nations.  
*Quart. J. exp. Physiol.*—Quarterly Journal of Experimental Physiology.  
*Quart. J. Med.*—Quarterly Journal of Medicine.  
*Quart. J. Pharm.*—Quarterly Journal of Pharmacy and Pharmacology.  
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*R.D.H.*—Pharmacopœia of the Royal Dental Hospital, London, 1926.  
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*R.L.O.H.*—Pharmacopœia of the Royal London Ophthalmic Hospital (Moorfields Eye Hospital), 1933.  
*R.N.H.*—Pharmacopœia of the Royal Northern Group of Hospitals, 1938.  
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*Rem.*—Remington's Practice of Pharmacy, 7th Edn., 1926.  
*Rep. Brit. Emp. Cancer Campgn*—Report of the British Empire Cancer Campaign.  
*Rep. Cancer Res. Fd.*—Report of the Imperial Cancer Research Fund.  
*Rep. Inst. med. Res. F.M.S.*—Report of the Institute for Medical Research, Federated Malay States.  
*Rep. med. Offr Minist. Hlth, Lond.*—Report of the Chief Medical Officer, the Ministry of Health.  
*Rep. med. Res. Coun., Lond.*—Report of the Medical Research Council.  
*Rep. metrop. Asylums Bd.*—Report of the Metropolitan Asylums Board.

- Rep. metrop. Wat. Bd.*—Report of the Metropolitan Water Board.  
*Rep. publ. Hlth. med. Subj., Lond.*—Report on Public Health and Medical Subjects, Ministry of Health.  
*Retail Chem.*—Retail Chemist.
- [81]—First Schedule to the Poisons Rules, 1935. Other Schedules are indicated by the corresponding numerical suffix.
- S.R.A., F.D., No. 2, Rev. 4.*—Service and Regulatory Announcements, Food and Drug No. 2 (Fourth Revision); issued by the United States Department of Agriculture, Food and Drug Administration, Nov., 1936.
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- S.V.*—saponification value.
- St. B. H.*—Pharmacopœia of St. Bartholomew's Hospital, 1936.
- St. G. H.*—Pharmacopœia of St. George's Hospital, 1927.
- St. J. H.*—Pharmacopœia of St. John's Hospital for Skin Diseases, 1934.
- St. M. H.*—Pharmacopœia of St. Mary's Hospital, 1934.
- St. Mark's H.*—Pharmacopœia of St. Mark's Hospital for Diseases of the Rectum and Colon, 1935.
- St. T. H.*—Pharmacopœia of St. Thomas' Hospital, 1935.
- St. Afr. med. J.*—South African Medical Journal.
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- Schweiz. med. Wschr.*—Schweizerische medizinische Wochenschrift.
- Sci. Rep. Cancer Res. Bd., Lond.*—Scientific Reports on the Investigations of the Imperial Cancer Research Fund.
- Science*—Science.
- Secret Remedies*—Secret Remedies, What they Cost and What they Contain.—British Medical Association (1909); also "More Secret Remedies" (1912).
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- Sp. gr.*—specific gravity.
- Spec. Rep. Food Invest. Bd., Lond.*—Special Report, Food Investigation Board, Department of Scientific and Industrial Research.
- Spec. Rep. Ser. med. Res. Comm.*—National Health Insurance, Medical Research Committee, Special Report Series.
- Spec. Rep. Ser. med. Res. Coun., Lond.*—Special Report Series, Medical Research Council, London.
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- Svensk farm. Tidskr.*—Svensk farmaceutisk Tidskrift.
- T.H.*—Pharmacopœia of the Golden Square Throat, Nose and Ear Hospital, 1935.
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- Trans. Brit. Soc. dent. Surg.*—Transactions of the British Society of Dental Surgeons.
- Trans. R. Soc. trop. Med. Hyg.*—Transactions of the Royal Society of Tropical Medicine and Hygiene.
- Trop. Dis. Bull.*—Tropical Diseases Bulletin.
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- U.F.C. '25*—Fourteenth Annual Report, United Fruit Co., Medical Dept., 1925.
- U.S.D.*—United States Dispensatory, 21st Edn., 1937.
- U.S.P. XI*—Pharmacopœia of the United States, 1935.
- U.S.P. XI Supp. I and II.*—Supplements I (1937) and II (1939) to the United States Pharmacopœia.
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- v/v*—volume in volume.
- v/w*—volume in weight.
- Vet. J.*—Veterinary Journal.
- Vic. Park*—City of London Hospital for Diseases of the Heart and Lungs, Victoria Park, E.2, 1926.

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*w/v*—weight in volume; *w/w*—weight in weight.  
*W.E.F.*—War Emergency Formulary, 1917—Addendum to the British Pharmaceutical Codex, 1911.  
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*Wynter Blyth*—Foods: Their Composition and Analysis, by the late A. Wynter Blyth and M. Wynter Blyth, 7th Edn., revised by H. E. Cox, 1927.  
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*Z. anal. Chem.*—Zeitschrift für analytische Chemie.  
*Z. angew. Chem.*—Zeitschrift für angewandte Chemie und Zentralblatt für technische Chemie. (Since 1932, continued as *Angewandte Chemie*.)  
*Z. ges. exp. Med.*—Zeitschrift für die gesamte experimentelle Medizin.  
*Z. Hyg. Infekt.Kr.*—Zeitschrift für Hygiene und Infektionskrankheiten.  
*Z. Immunforsch.*—Zeitschrift für Immunitätsforschung und experimentelle Therapie.  
*Z. klin. med.*—Zeitschrift für klinische Medizin.  
*Z. phys. Chem.*—Zeitschrift für physikalische Chemie und Untersuchung der Lebensmittel.

### PERCENTAGE AND GRAINS PER FLUID OUNCE EQUIVALENTS

%	Grains per fluid ounce	%	Grains per fluid ounce	%	Grains per fluid ounce
10.0	43.75	4.5	19.7	1.4	6.1
9.5	41.56	4.0	17.5	1.3	5.7
9.0	39.4	3.5	15.3	1.2	5.25
8.5	37.2	3.0	13.1	1.1	4.8
8.0	35.0	2.5	10.95	1.0	4.4
7.5	32.8	2.0	8.75	0.9	3.95
7.0	30.6	1.9	8.3	0.8	3.5
6.5	28.45	1.8	7.9	0.7	3.05
6.0	26.25	1.7	7.45	0.6	2.6
5.5	24.05	1.6	7.0	0.5	2.2
5.0	21.9	1.5	6.55	0.4	1.75

# WEIGHTS AND MEASURES APPROXIMATE EQUIVALENTS WEIGHTS. IMPERIAL TO METRIC.

grain	gramme	grain	gramme	grains	grammes
1000	= 0.000065	1	= 0.016	15	= 1.0
100	= 0.0003	1	= 0.02	20	= 1.2
200	= 0.0006	1	= 0.03	30	= 2.0
100	= 0.001	1	= 0.05	45	= 3.0
1	= 0.0013	1	= 0.06	60	= 4.0
1	= 0.0015	grains	gramme	90	= 6.0
1	= 0.002	1	= 0.1	120	= 8.0
1	= 0.0025	2	= 0.12	150	= 10.0
1	= 0.003	3	= 0.2	180	= 12.0
1	= 0.004	4	= 0.25	1 ounce	
1	= 0.005	5	= 0.3	(av.)	= 15.0
1	= 0.006	6	= 0.4	1 "	= 30.0
1	= 0.008	8	= 0.5	(or nearer 28.35)	
1	= 0.01	10	= 0.6	1 pound	
1	= 0.012	12	= 0.8		= 453.59

## WEIGHTS. METRIC TO IMPERIAL.

1 kilogramme	..	..	..	= 2 lb.	3½ oz.
500 grammes	..	..	..	= 1 "	1½ "
100 "	..	..	..	= 3½ oz.	
25 "	..	..	..	= 7 "	
10 "	..	..	..	= 15.43 grains	
1 "	..	..	..	= 7.7 "	
½ "	..	..	..	or 500 milligrammes	

## MEASURES. IMPERIAL TO METRIC.

minim	ml.	minims	ml.	fluid oz.	ml.
1	= 0.03	15	= 1.0	1	= 30.0
1	= 0.06	20	= 1.2	fluid ozs.	
minims		25	= 1.5	2	= 60.0
2	= 0.12	30	= 2.0	4	= 115.0
3	= 0.2	40	= 2.5	5	= 140.0
4	= 0.25	45	= 3.0	6	= 170.0
5	= 0.30	60	= 4.0	8	= 230.0
6	= 0.4	90	= 6.0	10	= 280.0
8	= 0.5	120	= 8.0	20	= 568.0
10	= 0.6	240	= 15.0	gallon	litres
12	= 0.8			1	= 4.536

## MEASURES. METRIC TO IMPERIAL.

1 ml.	..	..	= 15 (nearer 17) minims.
1 litre	..	..	= 1 pint 15 fl. oz. approx.

## MEASURES OF LENGTH.

1 micromillimetre	= 1/1000000 millimetre, usually represented by mμ.
1 micron	= 1/1000 millimetre, or 1 micrometre " " μ.
1 millimetre	= 0.03937 inch.
1 centimetre	= 0.3937 inch.
1 decimetre	= 3.937 inches.
1 metre	= 39.370113 inches or 1 yard 3.37 inches nearly.

## MISCELLANEOUS EQUIVALENTS

1 minim = the volume at 16.7°C. of 0.9114583 grain of water.

1 fluid drachm = the volume at 16.7°C. of 54.6875 grains of water.

1 fluid ounce = the volume at 16.7°C. of 437.5 grains of water.

109.7143 minims (taken as 110 minims) = the volume at 16.7°C. of 100 grains of water.

1 grain per gallon =  $\frac{100}{7}$  parts per million.

1 part per million =  $\frac{7}{100}$  grains per gallon.

1 pound = 7000 grains.

$\frac{1}{100}$  grain per lb. = approx. 1.4 parts per million.

A gallon of water weighs 10 pounds.

A "Corbyn" = 40 ounces fluid (1 quart).

A "Winchester" quart = 80 ounces fluid ( $\frac{1}{2}$  gallon).

## PROPORTIONAL DOSES ACCORDING TO AGE

The following are some of the methods that have been proposed for calculating the dose for a child from that for an adult.

## Gaubius' Method.

Under 1 year	will require	$\frac{1}{12}$	the adult dose
" 2 years	"	"	"
" 3 "	"	"	"
" 4 "	"	"	"
" 7 "	"	"	"
" 14 "	"	"	"
" 20 "	"	"	"
From 21 to 60 years will require the full adult dose.			

## Young's Formula.

$\frac{\text{Age}}{\text{Age} + 12}$ . Thus for 8 years, the dose required is

$\frac{8}{8 + 12} = \frac{2}{5}$  of the adult dose. The formula applies only to children under 12.

**Dilling's Formula.** This method represents an attempt to correlate dose with body weight. Dilling states that the fraction  $\frac{\text{age}}{20}$  approximates closely to the weight curve, between the ages of 4 and 20.

**Clark's Formula.**  $\frac{\text{Body weight in lb.}}{150}$

**Fried's Formula.**

For infants,  $\frac{\text{age in months}}{150}$

**Dosage for the Aged.** Above the age of 60, an inverse gradation must be observed. The following are the fractions suggested (Dixon's *Manual of Pharmacology*, 8th Edn., revised by W. A. M. Smart, 1936):—

Aged 60 to 70:	$\frac{1}{2}$	the usual adult dose.
" 70 to 80:	$\frac{1}{3}$	"
" 80 to 90:	$\frac{1}{4}$	"
Over 90:	$\frac{1}{5}$	"

## CALCULATION OF A DOSE FOR MAN FROM KNOWN DOSE FOR AN ANIMAL

The rate of catabolism of an animal is not proportional to size or weight but approximately to the body surface. Surfaces of solids of the same shape are proportional to the two-thirds power of their volumes (*i.e.*, the cube root of the square of the volumes). Since the specific gravity of animals varies only slightly, their body surface is a function of the two-thirds power of their weight. This relation is expressed by Meeh's Formula,  $S = k(W)^{\frac{2}{3}}$ , where  $S$  is the surface in square centimetres,  $W$  is the weight in grammes, and  $k$  is a factor which is nearly constant for all animals of the same shape.

(Rubner gives the following values for  $k$ : Man, 12.3; Dog, 10.3—11.2; Rabbit, 12.0—12.9; Cat, 9.9; Guinea Pig, 10.5.)

*A formula for calculating the dose for man.* This assumes that  $k$ , the factor, is the same for man and animals, and is approximate only, as the values actually differ somewhat.

If the dose for man and the animal should be proportional to their rates of catabolism, *i.e.*, to their body surface, then:

$$\frac{DM}{DA} = \frac{SM}{SA} = \frac{\kappa(M)^{\frac{2}{3}}}{\kappa(A)^{\frac{2}{3}}}$$

$DM$  = Dose for man in g.

$DA$  = Dose for adult test animal in g.

$SM$  = Body surface of man.

$SA$  = Body surface of animal.

$M$  = Wt. of man in g.

$A$  = Wt. of test animal in g.

$$\text{Hence } DM = \frac{(M)^{\frac{2}{3}}}{(A)^{\frac{2}{3}}} \times DA = \frac{1590 \times DA}{(A)^{\frac{2}{3}}}$$

for a 10-stone (63.5 kilo) man.

Thus, a dose of 1 g. per kilo for an animal is equivalent to 15.9 g., not 63.5 g., for a 10-stone man.

No exact method of calculating the corresponding dose for man from that of an animal is known. The figure obtained by the above formula is useful as a guide, but allowance must still be made for the fact that man may be more sensitive to the drug than the animal.

## TRANSPOSITION TABLE OF DOSES STATED FOR MAN IN MG. PER KILO TO MAN'S WEIGHT

Mg. per kilo.

1	=	1 grain (0.065 g.)	for a 10-stone (63.5 kilo) man
5	=	5 " (0.32 g.)	" " " "
10	=	10 " (0.64 g.)	" " " "
50	=	50 " (3.20 g.)	" " " "

As 5 mg. per kilo more nearly = 4.9 grains (0.318 g.) per 10-stone man, the above figures contain a 2% error in excess.

## THERMOMETRIC EQUIVALENTS

°C.	°F.	°C.	°F.	°C.	°F.	°C.	°F.	°C.	°F.
—	—	9	48.2	62	143.6	117	242.6	172	341.6
40	40.0	10	50.0	63	145.4	118	244.4	173	343.4
39	38.2	11	51.8	64	147.2	119	246.2	174	345.2
38	36.4	12	53.6	65	149.0	120	248.0	175	347.0
37	34.6	13	55.4	66	150.8	121	249.8	176	348.8
36	32.8	14	57.2	67	152.6	122	251.6	177	350.6
35	31.0	15	59.0	68	154.4	123	253.4	178	352.4
34	29.2	16	60.8	69	156.2	124	255.2	179	354.2
33	27.4	17	62.6	70	158.0	125	257.0	180	356.0
32	25.6	18	64.4	71	159.8	126	258.8	181	357.8
31	23.8	19	66.2	72	161.6	127	260.6	182	359.6
30	22.0	20	68.0	73	163.4	128	262.4	183	361.4
29	20.2	21	69.8	74	165.2	129	264.2	184	363.2
28	18.4	22	71.6	75	167.0	130	266.0	185	365.0
27	16.6	23	73.4	76	168.8	131	267.8	186	366.8
26	14.8	24	75.2	77	170.6	132	269.6	187	368.6
25	13.0	25	77.0	78	172.4	133	271.4	188	370.4
24	11.2	26	78.8	79	174.2	134	273.2	189	372.2
23	9.4	27	80.6	80	176.0	135	275.0	190	374.0
22	7.6	28	82.4	81	177.8	136	276.8	191	375.8
21	5.8	29	84.2	82	179.6	137	278.6	192	377.6
20	4.0	30	86.0	83	181.4	138	280.4	193	379.4
19	2.2	31	87.8	84	183.2	139	282.2	194	381.2
18	0.4	32	89.6	85	185.0	140	284.0	195	383.0
17-778	0.0	33	91.4	86	186.8	141	285.8	196	384.8
—	—	34	93.2	87	188.6	142	287.6	197	386.6
17	1.4	35	95.0	88	190.4	143	289.4	198	388.4
16	3.2	36	96.8	89	192.2	144	291.2	199	390.2
15	5.0	37	98.6	90	194.0	145	293.0	200	392.0
14	6.8	37.5	99.5	91	195.8	146	294.8	201	393.8
13	8.6	38	100.4	92	197.6	147	296.6	202	395.6
12	10.4	39	102.2	93	199.4	148	298.4	203	397.4
11	12.2	39.5	103.1	94	201.2	149	300.2	204	399.2
10	14.0	40	104.0	95	203.0	150	302.0	205	401.0
9	15.8	41	105.8	96	204.8	151	303.8	206	402.8
8	17.6	42	107.6	97	206.6	152	305.6	207	404.6
7	19.4	43	109.4	98	208.4	153	307.4	208	406.4
6	21.2	44	111.2	99	210.2	154	309.2	209	408.2
5	23.0	45	113.0	100	212.0	155	311.0	210	410.0
4	24.8	46	114.8	101	213.8	156	312.8	211	411.8
3	26.6	47	116.6	102	215.6	157	314.6	212	413.6
2	28.4	48	118.4	103	217.4	158	316.4	213	415.4
1	30.2	49	120.2	104	219.2	159	318.2	214	417.2
0	32.0	50	122.0	105	221.0	160	320.0	215	419.0
+	+	51	123.8	106	222.8	161	321.8	216	420.8
1	33.8	52	125.6	107	224.6	162	323.6	217	422.6
2	35.6	53	127.4	108	226.4	163	325.4	218	424.4
3	37.4	54	129.2	109	228.2	164	327.2	219	426.2
4	39.2	55	131.0	110	230.0	165	329.0	220	428.0
5	41.0	56	132.8	111	231.8	166	330.8	221	429.8
6	42.8	57	134.6	112	233.6	167	332.6	222	431.6
7	44.6	58	136.4	113	235.4	168	334.4	223	433.4
8	46.4	59	138.2	114	237.2	169	336.2	224	435.2
		60	140.0	115	239.0	170	338.0	225	437.0
		61	141.8	116	240.8	171	339.8	226	438.8

\* Clinical Limits.

The Réaumur scale (with zero at freezing-point of water and the boiling-point of water being 80°) is now little used.

To convert C. into F. multiply by  $\frac{9}{5}$  and add 32. To transpose F. into C. subtract 32 and multiply by  $\frac{5}{9}$ . To convert C. into R. multiply by  $\frac{4}{5}$ . To convert R. into C. multiply by  $\frac{5}{4}$ . To convert F. into R. subtract 32 and multiply by  $\frac{4}{9}$ . To convert R. into F. multiply by  $\frac{9}{4}$  and add 32.

## INTERNATIONAL ATOMIC WEIGHTS, 1940

Element.	Sym- bol.	Atomic Weight.	Element.	Sym- bol.	Atomic Weight.
Aluminium ..	Al	26.97	Molybdenum ..	Mo	95.95
Antimony ..	Sb	121.76	Neodymium ..	Nd	144.27
Argon ..	A	39.944	Neon ..	Ne	20.183
Arsenic ..	As	74.91	Nickel ..	Ni	58.69
Barium ..	Ba	137.36	Nitrogen ..	N	14.008
Beryllium ..	Be	9.02	Osmium ..	Os	190.2
Bismuth ..	Bi	209.00	Oxygen ..	O	16.0000
Boron ..	B	10.82	Palladium ..	Pd	106.7
Bromine ..	Br	79.916	Phosphorus ..	P	30.98
Cadmium ..	Cd	112.41	Platinum ..	Pt	195.23
Calcium ..	Ca	40.08	Potassium ..	K	39.096
Carbon ..	C	12.010	Praseodymium ..	Pr	140.92
Cerium ..	Ce	140.13	Radium ..	Ra	226.05
Cesium ..	Cs	132.91	Radon ..	Rn	222.00
Chlorine ..	Cl	35.457	Rhenium ..	Re	186.31
Chromium ..	Cr	52.01	Rhodium ..	Rh	102.91
Cobalt ..	Co	58.94	Rubidium ..	Rb	85.48
Columbium ..	Cb	92.91	Ruthenium ..	Ru	101.7
Copper ..	Cu	63.57	Samarium ..	Sm	150.43
Dysprosium ..	Dy	162.46	Scandium ..	Sc	45.10
Erbium ..	Er	167.2	Selenium ..	Se	78.96
Europium ..	Eu	152.0	Silicon ..	Si	28.06
Fluorine ..	F	19.00	Silver ..	Ag	107.880
Gadolinium ..	Gd	156.9	Sodium ..	Na	22.997
Gallium ..	Ga	69.72	Strontium ..	Sr	87.63
Germanium ..	Ge	72.60	Sulphur ..	S	32.06
Gold ..	Au	197.2	Tantalum ..	Ta	180.88
Hafnium ..	Hf	178.6	Tellurium ..	Te	127.61
Helium ..	He	4.003	Terbium ..	Tb	159.2
Holmium ..	Ho	163.5	Thallium ..	Tl	204.39
Hydrogen ..	H	1.0080	Thorium ..	Th	232.12
Indium ..	In	114.76	Thulium ..	Tm	169.4
Iodine ..	I	126.92	Tin ..	Sn	118.70
Iridium ..	Ir	193.1	Titanium ..	Ti	47.90
Iron ..	Fe	55.85	Tungsten ..	W	183.92
Krypton ..	Kr	83.7	Uranium ..	U	238.07
Lanthanum ..	La	138.92	Vanadium ..	V	50.95
Lead ..	Pb	207.21	Xenon ..	Xe	131.3
Lithium ..	Li	6.940	Ytterbium ..	Yb	173.04
Lutecium ..	Lu	174.99	Yttrium ..	Y	88.92
Magnesium ..	Mg	24.32	Zinc ..	Zn	65.38
Manganese ..	Mn	54.93	Zirconium ..	Zr	91.22
Mercury ..	Hg	200.61			





*The Editor would welcome any suggestions regarding the subject matter or arrangement of the work, from Medical Men, Pharmacists, or Analysts.*

## ACACIA

*B.P., U.S.P. XI, Fr. Cx., P. Helv. V, P. Jap. V, etc.*

*Syn. ACACIÆ GUMMI, GOMME ARABIQUE, GOMME DU SÉNÉGAL.*

A dried exudation from the stem and branches of *A. senegal* Willd. (*Leguminosæ*), and other species, either colourless or with yellowish tint.

The gum contains arabin which consists of a mixture of Ca, Mg and K arabinates. On hydrolysis it yields arabinose and other sugars.

**Soluble** almost completely in water; insoluble in alcohol.

**Incompatibles.** Alcohol, mineral acids, borax, ferric salts, oxalic acid and most lead salts. Bismuth carbonate should not be suspended with acacia mucilage; tragacanth is better.

**Uses.** For intravenous injection to raise blood pressure after loss of blood, especially that resulting from surgical shock. The solution has the same viscosity as the blood, and a content of colloids with osmotic pressure equal to that of the blood, hence it does not leave the circulation rapidly. It causes an increase in the plasma and blood volumes, but a decrease in the serum proteins, and repeated injections are not advisable. Its use is being largely replaced by blood transfusions or dextrose-saline injections.

Powdered acacia is used as an emulsifying agent for oils, the usual proportion being about 1 of gum to 4 of a fixed oil or 2 of a volatile oil. Less suffices in some cases. For its use as a pill excipient, *vide* *Pilulæ*.

Dangers of 6% gum-saline solution are: injury to the hepatic parenchyma with enlargement of the liver and diminished excretion of bile salts and pigment and diminution in urine volume. Repeated injections are much more apt to cause harm, particularly from depression of serum proteins and damage to the polygonal cells of the liver. In an emergency, however, when it is not possible to give a blood transfusion immediately, the intravenous injection of acacia solution may be regarded as a temporary substitute. Its use is more justifiable in shock than in severe hæmorrhage.—J. D. Stewart, *New Engl. J. Med.*, 1936, 215, 56.

Plasma and blood volumes are increased after acacia is given intravenously to dogs, with a proportionately greater decrease in the total proteins. The plasma volume returns to normal quickly, but the protein regeneration is delayed. The albumin, globulin and fibrinogen factors are all decreased and regenerate relatively slowly. The fibrinogen may become very low and cause considerable delay in clotting and prolongation of bleeding if large amounts of acacia are given. Acacia given intravenously causes lowering of cholesterol to about half the normal value with a slow increase to normal, while hæmoglobin, cell volume, and red blood cell count decrease markedly and regenerate slowly. The intravenous administration of acacia is contraindicated in nephrosis, when one considers that the ultimate recovery of the patient is dependent upon his ability to restore his level of serum protein to normal.—R. L. Jackson and L. Frayser, *J. Pharmacol.*, 1939, 65, 440.

**BURNS.** The secondary shock of burns is best treated by intravenous injection of 6% gum saline solution—normal saline or dextrose-saline will do more harm than good.—W. C. Wilson, *Practitioner*, i/1936, 398.

**DIABETIC COMA.** Desperate cases recovered with large quantities of fluid intravenously—hypertonic saline and acacia solution (7%).—R. D. Lawrence, *Brit. med. J.*, i/1930, 690.

**OBSTETRIC SHOCK** treated with definite benefit. Many lives saved by early use. Should be employed more extensively.—L. M. Randall, *J. Amer. med. Ass.*, ii, 1929, 847.

**Injectio Sodii Chloridi et Acaciæ (B.P.).** Acacia 60 g., sodium chloride 9 g., sterilised water to 1000 ml. The solution is autoclaved at 121° to 122° for one hour, cooled, filtered and again autoclaved.

A four-fold concentrated solution of acacia-saline may be prepared from the following formula and directions. Gum acacia, in tears, 1250 g., sodium chloride 187.5 g., water to 5000 ml. Dissolve the sodium chloride in the water, boil and add the gum acacia. Stir till dissolved. Strain through fine muslin, adjust the pH to 7.0 to 7.2, cover the container with parchment paper and autoclave at 15 lbs. pressure for 90 minutes. Add 200 g. of kieslguhr to the solution, filter, rinse the flask with a little water and filter this. An accurate dilution figure is calculated from the sodium chloride content of the filtrate, a small quantity of which is diluted and assayed. The filtrate is then filled in suitable volumes into ampoules, sealed, and autoclaved at 10 lbs. pressure for 30 minutes. Or the filtrate may be diluted with water to contain 0.9% of sodium chloride, the pH adjusted to 7.0 to 7.2, filtered, put in suitable containers and autoclaved at 5 lb. pressure for 45 minutes or at 10 lb. for 30 minutes.—H. Gartside, *Quart. J. Pharm.*, 1939, 550.

Replacement of gum arabic in preparation of emulsions may be accomplished by the use of galactose or pectin. Casein also gives good emulsions, but does not keep well.—F. V. Ivenor and G. A. Kleibs, per *Brit. chem. Abstr. (B)*, 1939, 1290.

**Ampulla Acaciæ et Sodii Chloridi (L.C.C.).** Acacia 6%, sodium chloride 0.9%, in sterilised water to 500 ml. (17½ fl. oz.).

**Solutio Salina cum Acacia (U.C.H.).** has 0.91% of sodium chloride and 6% of acacia in distilled water.

### **Mucilago Acaciæ (B.P.).**

**Dose.**—1 to 4 drachms (4 to 16 ml.). Acacia 4, washed to remove any adherent dust, dissolved in chloroform water 6. This quantity measures about 8½. *Fr. Cx.* uses powdered acacia 1, water 1.

**Mucilago Acaciæ (U.S.P. XI).** *Average dose.*—½ ounce (15 ml.).

Acacia 35% w/v and sodium benzoate 1% in water.

**Mucilago Gummi Arabici (P. Jap. V).** Acacia 1, water 2.

**Pulvis Acaciæ Compositus.** Acacia 1, tragacanth 1. A useful pill excipient.

### **Syrupus Acaciæ (B.P.C.).**

**Dose.**—1 to 4 drachms (4 to 16 ml.). Mucilage of acacia 1, syrup 3. A demulcent for use in cough mixtures. Must be freshly prepared.

**Sirop de Gomme (Fr. Cx.).** Washed acacia 10, sucrose 56, water 34, all by weight.

**Potion Gommeuse (Fr. Cx.).** Acacia powder 1, syrup 3, orange flower water 1, by weight, with water to 15 parts by volume.

**Gummi Arabicum Desenzymatum (P. Helv. V)** is obtained by evaporating the mucilage, drying and powdering the residue; the oxydases are thus destroyed.

**Gummi Indici.** *Syn.* GHATTI GUM. From *Anogeissus latifolia* (Combretaceæ). Indian gum is used technically for the same purposes as acacia. **Mucilago Gummi Indici**, 1 to 3 of water, is used in place of mucilage of acacia in India and the Eastern Colonies.

**Acaciæ Cortex (B.P.C.).** The dried bark of *A. arabica* (Babul bark) and *A. decurrens* (Wattle bark) (Leguminosæ). **Decoctum Acaciæ Corticis** 6%, *dose*—½ to 2 fluid ounces; used occasionally as astringent internally or in gargles.

## ACETANILIDUM

### ACETANILIDUM

*B.P.C.*, *Fr. Cx.*, *P. Jap. V*, *P. Helv. V*, *U.S.P. XI*, *P. Dan.*, etc.  
 $C_6H_5NH \cdot CO \cdot CH_3 = 135 \cdot 1$ .

*Syn.* ANTIFEBRIN, PHENYLACETAMIDE.

[P1] "*Acetanilide; alkyl acetanilides.*"

[S3] "*Acetanilide; alkyl acetanilides—in substances not being preparations for the treatment of human ailments.*"

*Dose.*—2 to 5 grains (0·12 to 0·3 g.). Larger doses are sometimes given, but idiosyncrasy may exist. *P. Helv. V* and *Fr. Cx.* have maximum daily dose of 15 gr. *U.S.P. XI* average dose 3 gr. May be given in cachets or suspended by compound tragacanth powder.

Prepared by the action of glacial acetic acid on aniline. In small white odourless glittering crystals which produce a burning sensation on the tongue. M.p. 113° to 115°.

*Soluble* 1 in 220 of water, 1 in 22 of boiling water, slightly in glycerin, 1 in 3·5 of alcohol 90%, 1 in 5 of chloroform, 1 in 12 of ether, and readily soluble in benzene.

*Incompatible* with aspirin, chloral hydrate, menthol and phenazone.

*Antidotes.* Empty stomach by stomach tube or emetic. Keep patient lying down and warm. Give aromatic spirit of ammonia, 1 dr., in 4 oz. of water. Strychnine,  $\frac{1}{4}$  gr., hypodermically. Oxygen inhalations. Saline infusion with dextrose for collapse.

Tolerance to the drug is built up after continued use. For occasional use, for headache or lassitude, acetanilide is a powerful analgesic preparation of great value, but if it is abused there is actually a tendency towards production of headache with the resulting establishment of a vicious circle and the possibility of chronic acetanilide poisoning. A case described.—A. Leslie, *J. Amer. med. Ass.*, ii/1939, 2229.

Chronic acetanilide poisoning (cyanosis) in a woman of 55 who had been taking three powders a day for a year for the relief of headache, the powders consisting of acetanilide and phenazone 4 gr. of each, and caffeine 2 gr.—T. N. Morgan and A. G. Anderson, *Brit. med. J.*, ii/1940, 187.

*Pharmacology.* The action of acetanilide is due to the formation of *p*-aminophenol in the organism, and the drug is excreted in this form in the urine. Large doses or continued use result in the formation of methæmoglobin, leading to cyanosis. Idiosyncrasy sometimes occurs, cyanosis resulting from small doses. Chronic poisoning is indicated by weakness, dyspnoea, sweating, hot flushes, mental depression and rapid heart; sometimes erythematous rashes occur.

Sodium bromide slightly antagonises the antipyretic action of acetanilide. Caffeine raises the temperature of fevered rats and also antagonises the antipyretic action. Sodium bromide and caffeine together antagonise to a large extent its antipyretic action.—P. K. Smith and W. E. Hambourger, *J. Pharmacol.*, 1935, 55, 205.

*Uses.* Antipyretic and analgesic. Useful in neuralgia, migraine, sciatica and dysmenorrhœa. Applied externally as a dusting powder it relieves the pain of ulcers, but toxic symptoms may occur owing to absorption. Relieves the darting pains of locomotor ataxy.

[P1] **Pulvis Acetanilidi Compositus (B.P.C.).**

*Dose.*—3 to 5 grains (0.2 to 0.3 g.).

Acetanilide 7, caffeine 1, sodium bicarbonate 2.

[P1] **Tabellæ Acetanilidi Compositæ (B.P.C.).** Contain acetanilide 2 gr., caffeine  $\frac{1}{2}$  gr., and sodium bicarbonate 1 gr.

[P1-S1] **Tabellæ Acetanilidi Compositæ cum Codeina (B.P.C.).** As the preceding, with the addition of codeine  $\frac{1}{8}$  gr.

[P1] **Phenalgin (Eina Chemical Co., London; Pearson, Mitcham).** *Dose.*—5 to 15 grains (0.3 to 1 g.). A mixture with acetanilide as the active base, as an antipyretic and hypnotic. Tablets and gelatin (hard) capsules, 5 grains.

[P1] **Methylacetanilidum (B.P.C., Fr. Cx.).** *Syn.* EXALGIN.  $C_6H_5N(CH_3)OC \cdot CH_3 = 149.1$ .

*Dose.*— $\frac{1}{2}$  to 2 grains (0.03 to 0.12 g.) in solution, cachets or pills. In colourless crystals, with a slight saline taste.

An analgesic, anti-neuralgic, antipyretic (only in unsafe doses). Toxic doses cause paralysis of respiratory organs.

*Soluble* 1 in 60 of water, freely in alcohol, 1 in 10 of ether, 1 in 2 of chloroform.

*Incompatible* with salicylic acid.

*Antidotes.* Treat as for poisoning by acetanilide.

**Anilinum (B.P.C.).** *Syn.* MONOPHENYLAMINE.  $C_6H_5NH_2 = 93.1$ .

A colourless (when freshly distilled) oily liquid, with sp. gr. 1.027. Of burning taste, miscible with alcohol and oils, soluble 1 in 37 of water.

*Antidotes.* Empty stomach by stomach tube or emetic. Fresh air, artificial respiration, oxygen inhalations. Strychnine,  $\frac{1}{4}$  gr., hypodermically. Saline infusion. Venesection followed by blood transfusion.

Aniline has a direct effect on the heart muscle, producing arrhythmia and heart-block. Intoxication may be produced either by absorption *per os* or through the skin, and in its acute stage cardiac and not respiratory treatment is indicated.

Poisoning by a boy drinking less than 2 ml. of a water and aniline mixture. Final recovery under oxygen given through a nitrous oxide bag for 5 minutes at a time with intervals of 15 minutes, instead of constantly through a funnel—far better this way.—J. Inkster, *Lancet*, ii/1926, 752.

It has been shown that cases of acute aniline poisoning arise by absorption through the skin. Its immediate toxic effect is on the blood, and the symptoms are blue-grey discoloration of the lips, ears and cheeks. With concentrations of 1 part of aniline vapour in 10,000 to 1 part in 6000, serious disturbances occur after 1 hour's exposure.—per *Analyst*, 1940, 162.

Paranitroaniline, rubbed on the body of a coolie, caused death due to absorption through the skin.—per *Analyst*, 1939, 679.

**Paraphenylenediamine.**  $C_6H_4(NH_2)_2 = 108.1$ .

[P2] "Phenylene diamines; toluene diamines; other alkylated-benzene diamines; their salts."

[S3] "Phenylene diamines; toluene diamines; other alkylated-benzene diamines; their salts—in substances other than preparations for the dyeing of hair."

[S7] Preparations for the dyeing of hair containing phenylene

## ACETANILIDUM

*diamines or toluene diamines or other alkylated-benzene diamines or their salts must be labelled with the words "Caution. This preparation may cause serious inflammation of the skin in certain persons and should be used only in accordance with expert advice," instead of the word "Poison."*

Prepared by nitrating acetanilide and subsequent reduction with tin and hydrochloric acid. In white or reddish crystals soluble in water, alcohol and chloroform. M.p. 140°.

In cases of poisoning by paraphenylenediamine dyes, oedema of head, neck, tongue, eyelids and face is the first stage; skin eruptions, eczema, nausea or nervous symptoms, sleeplessness, dizziness, weakness, etc., or impairment of vision may follow.

**Hair Dyes.**—Before applying, the sebum must be removed. 1% approx. of ammonia is said to be safe, but 10% injurious. Lead dyes (*e.g.*, lead acetate and sodium thiosulphate) are dangerous, as also are silver, *e.g.*, pyro, amido and silver nitrate. Pure henna dye is harmless, though penetrating the cortex, as also Henna-reng (henna and indigo). As to the paraphenylenediamine group, toxic effects are both local and general. **Sabouraud-Rousseau's Test** is used as a sensitisation test. The skin over the mastoid process is cleaned with alcohol and then the dye and its oxidant applied. When dry cover with flexible collodion. After 24 hours remove collodion and wash with soap and water. If patient is sensitive a mild reaction will have formed. If dermatitis is caused in use as hair dye, or from furs, a simple calamine lotion containing 2% of ichthammol should be used. *Do not attempt to remove the dye by hydrogen peroxide or thiosulphate.*—R. M. B. Mackenna, *Brit. med. J.*, i/1930, 899. Some of these remarks are criticised by A. Mahony-Jones, *ibid.*, 979.

A case of systemic poisoning, with death from sub-acute atrophy of the liver, in a girl aged 21, a hairdresser's assistant. There was no skin affection traceable to the dye. Rubber gloves were used when applying the dye, and the gloves removed for the subsequent shampoo. The staining of the hands was removed with hydrogen peroxide, which was possibly a contributory cause, as it has been stated that it is most dangerous to remove the dye from the hair by the use of hydrogen peroxide or sodium thiosulphate, as these measures only intensify the symptoms. It seems possible that the production of aniline is responsible for the toxic symptoms.—M. C. G. Israels and W. Susman, *Lancet*, i/1934, 509.

Paraphenylenediamine and other diamines in hair dyes may be detected by tests described by C. Griebel and F. Weiss (*see Analyst*, 1933, 417).

**Dyed Furs.** Fur workers and wearers of dyed fur are liable to be affected with dermatitis from this substance. Investigations show that paraphenylenediamine is almost the only dye used, since it has the advantage of being used cold. The fur is dipped in a 0.5% solution and then into hydrogen peroxide, when "Bandrowski's base" is formed. The fur is then washed in revolving drums. Complete removal of all unoxidised amine should be made compulsory.—*Yearb. Pharm.*, 1924, 524.

The result of investigating a large number of cases of fur dermatitis has shown that at least 45% of these cases were due to paraphenylenediamine-dyed furs. Examination of its oxidation products formed during the process of dyeing and of the dyed fur showed that a large amount of Bandrowski base may be formed on the fur, and that the final product of the dyeing is an azine combined with the protein in the fur. Paraphenylenediamine itself, and not any intermediate oxidation products, is stated to be the active irritant in fur dermatitis.—H. E. Cox, *Analyst*, 1934, 3; *see also ibid.*, 1933, 738.

A normal person may fail to react to a 10% solution of Ursol containing *p*-phenylenediamine, whereas dermatitis cases react to concentrations as low as 0.005%.—W. J. O'Donovan, *Brit. med. J.*, ii/1932, 294.

[P2-83-87] **Metaphenylenediamine Hydrochloride.** *Syn.* METADIAMINO BENZENE HYDROCHLORIDE.  $C_6H_4(NH_2)_2 \cdot HCl = 144.6$ .

This compound is considered more poisonous in furs than the

para compound. It is used for the determination of nitrites in water.

**Benzidine.** White or slightly reddish crystals, m.p. 128°. Slightly soluble in alcohol, ether and boiling water. Used as a reagent for detecting certain oxidising agents, especially the oxidase of blood.

### Phenylhydrazinæ Hydrochloridum.

$C_6H_5 \cdot NH \cdot NH_2, HCl = 144.6$ .

**Dose.**— $1\frac{1}{2}$  to 5 grains (0.1 to 0.3 g.). 2 gr. per day should rarely be exceeded, and frequently 2 gr. per week is sufficient. Dosage must be controlled by blood counts.

Colourless shining scales, readily soluble in water and alcohol. M.p. 240°. *Handle carefully, may produce eczema.*

Phenylhydrazine has a specific effect in destroying erythrocytes and is used therefore in polycythæmia. There is a marked reduction in blood volume directly proportional to destruction of the erythrocytes, and when anæmia has been produced a relative increase in plasma volume is noted. The action is delayed and may continue for two weeks after administration has been stopped. Administration should cease as soon as the effect is noticed until it is known how far the erythrocyte count will fall.

In advanced polycythemia vera should not be given, and only with extreme caution to those over 60, patients with marked arteriosclerosis, or advanced visceral injury. Such patients should be given only small doses, 0.1 or 0.2 g., and subsequent dosage determined by symptoms. Less advanced cases do well on 0.1 to 0.3 g. weekly, and the effect observed over several days. Patients who have had thrombosis should be treated cautiously. Ambulatory treatment best, every effort being made to keep circulation as free as possible. Frequent counts of red and white cells and estimations of serum bilirubin needed. As its action continues after withdrawal, it should be stopped before red cell count is normal. Marked rise in bilirubin means excessive blood destruction, and rising leucocyte count indicates great destruction of liver cells. Results transitory and merely palliative.—H. Z. Giffin and H. M. Connor, *J. Amer. med. Ass.*, i/1929, 1507; Hurwitz and Levitus, *ibid.*, i/1929, 1629.

It is always advisable to omit the drug when the red cell count approaches 6,000,000 per c.mm. Should the red cell fall become alarming, blood transfusion will arrest its progress, followed by liver extract. A case described in which four short courses were given without untoward effect, but a fifth produced a severe hæmolytic crisis.—A. M. Kennedy, *Brit. med. J.*, i/1934, 657.

**Acetylphenylhydrazine.**  $C_6H_5 \cdot HN \cdot NH(C_2H_5O)$ . *Syn.* PYRODIN, HYDRACETIN. In colourless crystals slightly soluble in water, has also been used.

Equally effective as phenylhydrazine in polycythæmia vera without producing toxic symptoms so readily in similar doses.—C. T. Stone, T. H. Harris and M. Bodansky, *J. Amer. med. Ass.*, ii/1933, 495.

Superior to phenylhydrazine hydrochloride in the treatment of polycythæmia vera. Of 14 cases treated, 9 were improved, 2 were not improved, and 3 died. The treatment given was 0.1 g. of acetylphenylhydrazine for two or three days in the course of a week; this was repeated for several weeks and the dose then increased gradually to 0.4 or 0.5 g.—M. R. McAlpine and K. E. Smith, *N.Y. St. J. Med.*, 1938, 101.

**Acidum Sulphanilicum.**  $C_6H_4(NH_2)SO_3H \cdot 2H_2O (1:4) = 209.2$ .

**Dose.**—10 to 20 grains (0.6 to 1.2 g.).

In small white crystals, slightly soluble in water. Used in Ehrlich's Diazo Test, now superseded by the Widal reaction.

**Sodii Sulphanilas.**  $C_6H_4(NH_2)SO_3Na \cdot 2H_2O = 231.2$ .

**Dose.**—5 to 15 grains (0.3 to 1 g.).

In white shining scales, easily soluble in water. Useful in acute catarrh, laryngitis, and otitis.



**Zinci Sulphanilas.** *Prop. Name.* NIZIN (*Burroughs Wellcome, London*).

White crystals soluble 1 in 6 of water, 1 in 250 of alcohol. Astringent and antiseptic. Solutions 1 in 500 to 1 in 250 are injected in leucorrhœa and gonorrhœa. In atrophic rhinitis the nasal fossæ may be packed with gauze dipped in 1 to 2% solution.

## ACIDUM ACETICUM

$\text{CH}_3\cdot\text{COOH} = 60\cdot03.$

**Acidum Aceticum Glaciale** (*B.P., U.S.P. XI*). Contains not less than 99% *w/w* of  $\text{CH}_3\cdot\text{COOH}$ . *Sp. gr.* 1·055 to 1·058. *P. Belg. IV, P. Jap. V, P. Ital. V* and *F. E. VIII* not less than 96%; *Fr. Cx.* and *P. Helv. V* 98 to 100%; *P. Dan.* 96%.

A colourless liquid or crystals melting at about 14·7° obtained as a product of the destructive distillation of wood, or synthetically. *B.p.* 118°.

**Antidotes.** Stomach tube and emetics must *not* be used. Give a pint of water to which has been added 4 tablespoonfuls of magnesium or calcium hydroxide, or 2 teaspoonfuls of soap dissolved in a pint of warm water. (Chalk, sodium bicarbonate or carbonate, well diluted, may be used in absence of magnesium oxide, but it is better to avoid the use of carbonates if possible because the evolution of carbon dioxide may rupture the weakened walls of the stomach.) Milk, white of egg, oil or other demulcents. Morphine,  $\frac{1}{4}$  gr. hypodermically, for shock.

**Uses.** It is applied to corns and warts. Has caustic action, but gives much pain. Psoriasis of a chronic type has been cured in a week or two by glacial acetic acid locally.

**Acidum Aceticum Aromaticum** (*B.P.C.*). *Syn.* AROMATIC VINEGAR. Glacial acetic acid about 74% *v/v*, with odorants. Used as a restorative.

**Acidum Aceticum** (*B.P.*). 32·5 to 33·5% *w/w*. *U.S.P. XI* is 36 to 37%; *P. Helv. V* 29·5 to 30·5%; *P. Dan.* 29·5%.

*Dose.*—5 to 15 minims (0·3 to 1 ml.).

*B.P.* has *sp. gr.* 1·044 to 1·045. *P. Austr., P.G. VI* and *P. Belg. IV* (30%) and *F.E. VIII* (30%) designate this acid "Dilutum."

**Incompatibles.** Alkalis (hydroxides, carbonates, etc.).

**Use.** Externally for ringworm and in liniments.

**Acetum Odoratum** (*B.P.C.*). *Syn.* TOILET VINEGAR. Acetic acid 1 in 8 with odorants.

**Acetum Officinale** (*Fr. Cx.*). White wine vinegar containing about 6% of acetic acid.

**Lotio Acidi Acetici** (*R.L.O.H.*). Acetic acid 25 m., sterilised water to 1 ounce. Relieves itching and irritation, *e.g.*, in spring catarrh.

**Vapor Acidi Acetici** (*T.H.*). Acetic acid and glacial acetic acid, equal parts. One teaspoonful to a pint of hot water as a sedative inhalation.

**Acidum Aceticum Dilutum** (*B.P., U.S.P. XI*). 5·7 to 6·3% *w/w*.

*Dose.*— $\frac{1}{4}$  to 1 drachm (2 to 4 ml.).

*Sp. gr.* about 1·008. (*Fr. Cx.* is 10% *w/w*.)

## THE EXTRA PHARMACOPŒIA

**Uses.** May be given as an antidote to poisoning by alkalis, and, largely diluted, is applied as a lotion for inflamed joints, etc., and to bathe the skin as a refrigerant in cases of fever. A 1 in 20 dilution of this dilute acid is used in the form of drops to relieve the conjunctival itching of spring catarrh.

**Acetic Anhydride.**  $(\text{CH}_3\text{CO})_2\text{O}=102\cdot05$ .

A colourless liquid with pungent odour, sp. gr. 1·080. B.p. 138°.

Obtained by interaction of anhydrous sodium acetate and acetyl chloride.

Is not employed medicinally, but is extensively used in chemical manufacture.

**Acetyl Chloride.**  $\text{CH}_3\cdot\text{COCl}=78\cdot5$ . A volatile liquid with intensely penetrating odour, boiling at 51°. Obtained by combining carefully glacial acetic acid 130, with phosphorus pentachloride 137, distilling, and redistilling the fraction passing over below 60°.

**Acetamide.**  $\text{CH}_3\cdot\text{CONH}_2=59\cdot05$ .

Deliquescent crystals, m.p. 82°, made by interaction of ammonia and acetyl chloride.

**Æthylis Acetas** (*B.P.C.*, *Fr. Cx.*, *P. Helv. V*). *Syn.* **ÆTHER ACETICUS** (*P. Jap. V*).  $\text{CH}_3\cdot\text{COOC}_2\text{H}_5=88\cdot06$ .

**Dose.**— $\frac{3}{4}$  to 1 drachm (3 to 4 ml.) for a single administration;  $\frac{1}{4}$  to  $\frac{1}{2}$  drachm (1 to 2 ml.) for repeated administration.

Contains not less than 90% *w/w* of ethyl acetate. Boiling-range 73·9° to 77·8°. Sp. gr. 0·900 to 0·907.

**Soluble** 1 in 15 of water; miscible with alcohol, ether, and chloroform.

Is used as an inhalation in laryngeal catarrh,  $\frac{1}{2}$  drachm to 1 pint of warm water (60°). Internally it is carminative, antispasmodic and diaphoretic. Is largely used as a solvent.

**Potassii Acetas** (*B.P.*, *U.S.P. XI*, *Fr. Cx.*).

$\text{CH}_3\cdot\text{COOK}=98\cdot12$ .

**Dose.**—15 to 60 grains (1 to 4 g.). *U.S.P. XI* average dose 15 grains.

Deliquescent white crystals, masses or powder. Diuretic, and uric acid solvent.

**Soluble** 2 in 1 of water, 1 in 2 of alcohol 90%.

**Uses.** Is given to render the urine alkaline and as a diuretic. Has mild diaphoretic and febrifuge properties.

**Incompatible** with acids and silver, mercury and iron salts.

[P] **Mistura Potassii Acetatis Composita** (*B.P.C.*).

*Syn.* **MISTURA DIURETICA**.

**Dose.**— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.).

Contains potassium acetate 20 gr., spirit of nitrous ether 30 m., and tincture of hyoscyamus 20 m., with juice of scopolarium in infusion of buchu to 1 oz.

**Mist. Diuret.** (*N.I.F.*).

Potassium acetate 15 gr., potassium nitrate 7½ gr., vinegar of squill 20 m., decoction of scopolarium to ½ oz.

**Sodii Acetas** (*B.P.C.*, *U.S.P. XI*, *P. Helv. V*, *P. Jap. V*).

$\text{CH}_3\cdot\text{COONa}\cdot 3\text{H}_2\text{O}=136\cdot07$ .

**Dose.**—5 to 20 grains (0·3 to 1·2 g.). *U.S.P. XI* average dose, 25 grains.

Colourless crystals or white powder, efflorescent in warm air. Soluble about 1 in 1 of water, with alkaline reaction, and about 1 in 35 of alcohol 90%.

**Uses.** To some extent as a diuretic and as rectal injection in uræmia instead of the bicarbonate. It is excreted as carbonate.

[P1-S1] **Thallii Acetas** (B.P.C.). *Syn.* THALLOUS ACETATE.  $\text{CH}_3\cdot\text{COOTl}=263\cdot4$ .

[P1] and [S1] "*Thallium, salts of.*"

**Dose.**—0·008 g. per kg. body-weight ( $\frac{2}{3}$  grain per pound), unless there is marked discrepancy between age and weight, in sweetened aqueous solution.

A white crystalline powder, m.p. about 131°.

**Antidotes.** Empty stomach by emetic or stomach tube. Give purgative dose of magnesium sulphate. Milk in copious draughts. Keep patient warm. Caffeine sodium benzoate, 2 gr. hypodermically, for shock. Saline intravenously. Intravenous injection of potassium iodide has been suggested. Sodium thiosulphate intravenously in daily doses, 20 ml. of 3% solution slowly (too large doses are to be avoided), promotes gradual elimination of thallium in the urine.

It was much advocated for epilation in ringworm, the direction being to administer it only to children who have not reached the age of puberty in dosage based on weight of the child, but owing to the numerous fatalities due to this treatment, its use has now been largely abandoned (*see* 20th Edn.).

**Acetonum** (B.P., U.S.P. XI, *Fr. Cx.*, *P. Jap. V*, *F.E. VIII*, *P. Helv. V*). *Syn.* DIMETHYLKETONE.  $\text{CH}_3\cdot\text{CO}\cdot\text{CH}_3=58\cdot05$ .

**Dose.**—60 to 90 minims (4 to 6 ml.) daily.

A colourless, light, inflammable, neutral liquid, with ethereal odour and camphoraceous taste, obtained by the dry distillation of acetates, also by the destructive distillation of wood and by a fermentation process from maize starch.

It is *miscible* with water, alcohol, ether, chloroform, and oils, and is a ready solvent of fats and resins, pyroxylin, celluloid and many other organic substances. It takes up about 25 times its volume of acetylene. Sp. gr. is 0·796 to 0·801; b.p. 56° to 58°. It is largely employed in the manufacture of chloroform. Acetone has been used in dyspnoea. It has also been given as an anthelmintic, and used for cleansing the skin prior to operation.

It occurs in small quantity as a normal constituent in the urine, also (frequently in large amount) in that of diabetics, *cf.* Vol. II.

**Acetophenonum.** *Syn.* HYPNONE, PHENYLMETHYLKETONE.  $\text{C}_6\text{H}_5\cdot\text{CO}\cdot\text{CH}_3=120\cdot0$ .

**Dose.**—1½ to 5 minims (0·1 to 0·3 ml.) in almond emulsion, or with mucilage or syrup and peppermint water, or in capsules containing ½ minim.

A colourless liquid, with odour of bitter almonds. Insoluble in water, but soluble in alcohol and oils. Used as an hypnotic it requires care.

**Benzophenonum.** *Syn.* DIPHENYLKETONE.  $(\text{C}_6\text{H}_5)_2\text{CO}=182\cdot1$ .

**Dose.**—3 to 8 grains (0·2 to 0·5 g.). White aromatic crystals. Has hypnotic properties.

**Acidum Pyrolignosum Crudum.** A brown acid liquid, the product of destructive distillation of wood. Contains acetic acid 5 to 13% (*P.G. VI* has minimum 8·4%; *P. Helv. V* 6 to 7%) according to the kind of wood used, also other acids—propionic, butyric, ~~and~~ also small quantities of methyl

alcohol, furfural, pyridine, creosote and resins. Has been employed locally for gangrene and has veterinary uses. It has antiseptic and preservative properties.

**Acidum Pyrolignosum Rectificatum.** Contains about 5% acetic acid. Of yellowish colour becoming darker on keeping. Occasionally ordered diluted 5 to 10% in mouth-washes and gargles.

**Acidum Trichloraceticum** (B.P., U.S.P. XI, P. *Helv.* V, P. *Ned.* V, P. *Jap.*, P. *Dan.*, F.E. VIII).  $\text{CCl}_3\cdot\text{COOH}=163\cdot4$ .

Prepared by chlorination of acetic acid, or by the action of fuming nitric acid on chloral hydrate.

In deliquescent crystals, m.p.  $55^\circ$  (lower if moist), b.p.  $195^\circ$ , very soluble in water, alcohol and ether.

**Uses.** Applied as a crystal or liquefied by the addition of the minimum amount of water, it is a quick escharotic for venereal and other warts. As a disinfectant lotion or gargle, 1 to 5% aqueous solution may be used. A solution of 1 part in 2 of glycerin has been employed as a caustic in chronic pharyngitis.

LARYNGEAL TUBERCULOSIS treated by trichloracetic acid.—*Brit. med. J. Epit.*, ii/1930, 7.

LEPROTIC LESIONS treated with applications of a solution—1 in 1 for centre of large thick nodules, 1 in 5 for painting on face, and 1 in 3 generally useful. Must not be too strong or brush too wet. When dry, skin should show a white powdery appearance, otherwise repeat second or third time. May be repeated after 10 days.—E. Muir, *Indian med. Gaz.*, May, 1926, 216.

RIGGS'S DISEASE—incipient stages. This acid applied to the gum after cleaning with hydrogen peroxide solution 10 or 20 volume, is a good remedy. Should be tried before sound teeth are sacrificed.

RODENT ULCER. A solution of trichloracetic acid, 3 drachms in 20 minims of water, applied. The acid should be washed off after about 3 minutes, and then for 24 hours no soap or water is allowed on the ulcer. The eschar usually peels off in about 22 days.—H. Leslie-Roberts, *Brit. med. J.*, i/1927, 794.

TONSILS, DISEASES OF. Where operative treatment is not permitted, the use of trichloracetic acid applied on a right-angled wool-carrier and passed deeply into the crypts, has been found of value in reducing the size of the tonsil and adding to the comfort of the patient.

**Acidum Monochloraceticum.**  $\text{CH}_2\text{Cl}\cdot\text{COOH}=94\cdot5$ .

Prepared by chlorination of acetic acid in presence of iodine at water-bath temperature, subsequently fractionating and reserving the  $180^\circ$ — $188^\circ$  fraction. Deliquescent white crystals, m.p.  $63^\circ$ , or liquefied. It blisters the skin, and is a caustic for warts and corns. Soluble with ease in water, alcohol and ether.

**Acidum Dichloraceticum.**  $\text{CHCl}_2\cdot\text{COOH}=128\cdot95$ .

A colourless caustic for venereal sores.

**Glycine.** *Syn.* AMINOACETIC ACID, GLYCOCOLL.

$\text{CH}_2\cdot\text{NH}_2\cdot\text{COOH}=75\cdot05$ .

**Dose.**—150 grains to 1 ounce (10 to 30 g.) per day, in two or three doses.

White crystals with sweet taste, *soluble* in water 1 in  $4\frac{1}{2}$ , slightly in alcohol, insoluble in ether. M.p.  $234^\circ$ .

**Uses.** Of value in the treatment of myasthenia gravis. The muscular weakness is connected with a failure to convert creatine into creatinine, for which the presence of an amino-acid is necessary. Glycine produces an increase in the output of creatinine and a drop in the excretion of creatine. Is effective in some cases of myasthenia gravis in which ephedrine fails. Other cases are benefited by the supplementary administration

of ephedrine,  $\frac{3}{4}$  to  $\frac{1}{2}$  gr., given 20 minutes later (the total daily amount should never exceed  $1\frac{1}{2}$  gr.).

**MYASTHENIA GRAVIS.** Patients responding well to glycine failed to respond to gelatin. In two cases gelatin was tried as a substitute for glycine, a dose of 45 g. daily being administered for 13 and 23 days respectively, but the treatment had to be discontinued because the myasthenic manifestations increased. It was found that patients suffering from myasthenia gravis showed a diminished digestion of gelatin *in vitro* with the juice obtained from the duodenum.—E. J. Maltby, *Canad. med. Ass. J.*, 1937, 272.

**Choline.**  $\text{HO}\cdot\text{N}(\text{CH}_3)_3\text{C}_2\text{H}_4\cdot\text{OH} = 121\cdot1$ .

A non-poisonous syrupy fluid. A decomposition product of lecithin. It stimulates intestinal movements.

Choline is essential for liver function; lack of it causes fatty degeneration. Dogs with the pancreas removed died in a few months when treated with insulin alone, but survived for years when fed with minced pancreas (which contains choline) in addition. Diabetes is a disorder of the liver rather than of the pancreas, and may be caused by an over-active liver due to disease or to deficiency of insulin; or to over-active pituitary, thyroid or adrenal glands.—C. H. Best, *Science (Suppl.)*, i/1935, 2112.

**Choline Chloride.** *Syn.* CHOLINE HYDROCHLORIDE.

$\text{Cl}\cdot\text{N}(\text{CH}_3)_3\text{C}_2\text{H}_4\cdot\text{OH} = 139\cdot6$ .

*Dose.*—10 grains (0·6 g.) intravenously.

Deliquescent needles soluble in water and alcohol.

*Uses.* The actions of choline resemble those of acetylcholine (*q.v.*), though its depressant action on the circulation is markedly less. It has been employed intravenously in doses of 10 g. in 180 ml. of normal saline in the treatment of paralytic ileus, the injection being given very slowly. It has also been used to a limited extent in the treatment of pulmonary tuberculosis, subcutaneous injections of  $\frac{1}{2}$  grain in 1 ml. of water being given on alternate days for an indefinite period.

**Bakolyse** (*Anglo-French Drug Co., London*). A sterile solution of amino-acids and creatinine for intramuscular or subcutaneous use in tuberculosis and all states of denutrition. *Dose.*—2 ml. every 3 or 4 days with a minimum of 20 injections.

**Blocholone** (*Robert & Carrière, Paris; Anglo-French Drug Co., London*). Solution of choline hydrochloride for injection. *Dose.*—1 ml. (=0·01 g.) subcutaneously every two days continuously. In the treatment of all forms of tuberculosis.

**Pacyl Tablets** (*Coates & Cooper, London*). *Dose.*—1 or 2 tablets twice or thrice daily, commencing with the smaller dosage—to be swallowed whole and followed with water.

A choline preparation, each tablet containing  $\frac{1}{12}$  grain (0·005 g.), employed to reduce blood pressure in arteriosclerosis, chronic nephritis and the climacteric.

**Sedicyl Tablets** (*Coates & Cooper, London*). *Dose.*—1 or 2 tablets three times daily—subsequently 2 tablets a day. A choline derivative used at the climacteric.

**Acetylcholine.**  $(\text{CH}_3)_3\text{N}(\text{OH})\cdot\text{C}_2\text{H}_4\cdot\text{COO}\cdot\text{CH}_3 = 163\cdot1$ .

Usually employed as **acetylcholine chloride** or **hydrochloride**,  $(\text{CH}_3)_3\text{N}\cdot\text{Cl}\cdot\text{C}_2\text{H}_4\cdot\text{COO}\cdot\text{CH}_3 = 181\cdot6$ . A white hygroscopic powder forming a stable solution in water.

*Dose.*— $\frac{3}{4}$  grain (0·05 g.) subcutaneously or intramuscularly, and  $1\frac{1}{2}$  grains (0·1 g.) the following day. If inadequate after 10 days, increase to 0·2 g. twice daily. Average course 15 days'

treatment per month for 2 or 3 months. *Dangerous intravenously and ineffective orally.*

**Uses.** Acetylcholine is a powerful vasodilator and cardiac depressant. Its vasodilator action is exerted mainly on the arteries and arterioles, and is most marked in the peripheral vascular areas. It is a stimulant of the vagus and sympathetic, and has a tonic action on smooth muscle; it also increases the lachrymal, salivary, and other secretions. Acetylcholine has been employed, usually in the form of the hydrochloride, in the treatment of a wide variety of conditions such as Raynaud's disease, intermittent claudication, trophic ulcers, senile and diabetic gangrene, post-operative distension and paralytic ileus, and (by subconjunctival injection) in spasm of the retinal arteries and chronic glaucoma, but, except in the two last-mentioned conditions, the results have been too variable, probably owing to the fact that acetylcholine is rapidly destroyed in the system by choline esterase. It has now been largely replaced by carbachol or acetyl- $\beta$ -methylcholine chloride, both of which are similar in action to acetylcholine, but are more stable and therefore more reliable.

The results of the administration of acetylcholine to man by intra-arterial, intravenous, intramuscular, or subcutaneous injection, are disappointing from the therapeutic point of view. Given by intravenous injection the effects are too brief, and by intramuscular or subcutaneous injection they are too uncertain. —F. R. Fraser, *Brit. med. J.*, ii/1938, 1249.

**EMBOLISM.** Subconjunctival injections of acetylcholine solution the best form of treatment for embolism of the retinal artery—4 minims on the lower temporal quadrant and 4 minims in the lower nasal quadrant, as far back as the equator of the globe.—H. C. Orr and J. H. Young, *Brit. med. J.*, i/1935, 1119.

**HEADACHE** following lumbar puncture can be readily relieved by hypodermic injection of 0.02 g. of acetylcholine. The dose may be repeated if necessary.—Lemaire and Bioy, per *Prescriber*, 1936, 89.

**HYPERPIESIS** without marked arterial change treated. Semi-permanent fall in blood pressure produced.—A. H. Douthwaite, *Brit. med. J.*, i/1930, 742.

**PARALYTIC ILEUS.** Most patients with severe post-operative distension, gas pains, and paresis of the bowels are considerably improved by administration of acetylcholine intramuscularly. In paralytic ileus it appears to be almost specific in curing the condition.—A. L. Abel, *Lancet*, ii/1933, 1252. Value confirmed by K. Heritage, *ibid.*, 1258.

**PAROXYSMAL TACHYCARDIA.** In 5 cases in which the drug was used *intravenously* in doses of 0.1 g. it stopped the paroxysmal tachycardia immediately, with little if any of the terrific side effects resulting from meclohyl.—K. H. Abott, *J. Amer. med. Ass.*, ii/1939, 1243.

**TOBACCO AMBLYOPIA.** Four cases received marked benefit from intramuscular injections of acetylcholine 0.1 g., given at first daily, and later once a week. It is suggested that the drug counteracts constriction of the arterioles due to nicotine poisoning.—H. C. Orr, *Brit. med. J.*, ii/1936, 69.

**Acécoline** (Lematte, Paris: Anglo-French Drug Co., London). A stable solution of acetylcholine hydrochloride in 1 ml. ampoules containing 0.02, 0.05, 0.1 and 0.2 g. *Average dose.*—0.1 g. twice daily, for 15 injections.

**Acécoplex** (Lematte, Paris: Anglo-French Drug Co., London). An ointment containing 2% of Acécoline with the addition of fenchone as an antiseptic. For the treatment of varicose ulcers, atonic wounds and dermatosis.

**Tonocholin** (Richter, London). Each 1 ml. ampoule contains 1.75 gr. of acetylcholine-bromine. *Dose.*—1 ml. (0.05 g.) subcutaneously or intravenously on alternate days.

**Pragmoline** (*Pharmaceutical Specialities (May & Baker) Ltd., London*). Acetylcholine bromide. Supplied in 1 ml. ampoules of a 12.5% solution. Given by deep subcutaneous injection, or intramuscularly, in hypertension, Raynaud's disease and tuberculous sweats.

[P1] **Hypotan** (*Lemaitre, Paris; Anglo-French Drug Co., London*). Methyl-acetylcholine bromide 0.005 g., bromocholine bromide 0.005 g., chloral hydrate 0.05 g. *Dose*.—4 to 6 tablets daily before meals for 15 days each month. In hypertension. Also supplied in 1 ml. ampoules.

**Carbacholum** (*B.P. Add. III*).

$\text{NH}_2\cdot\text{CO}_2\cdot\text{CH}_2\cdot\text{CH}_2\text{N}(\text{CH}_3)_3\text{Cl} = 182.6$ . *Prop. Name*. MORYL (*Savory & Moore, London*), CHORYL (*Pharmaceutical Products, London*).

(A foreign proprietary of similar composition was formerly marketed in this country under the registered trade name DORYL.)

*Dose*.—Orally  $\frac{1}{4}$  to  $\frac{1}{16}$  grain (0.001 to 0.004 g.); subcutaneously or intramuscularly  $\frac{1}{16}$  to  $\frac{1}{32}$  grain (0.00025 to 0.0005 g.). *It should never be used intravenously*.

Carbachol is carbamylcholine chloride, the urethane of choline, and it occurs as a white, odourless, crystalline powder, hygroscopic in moist air. M.p.  $210^\circ$  to  $212^\circ$  with decomposition.

**Soluble** 1 in 1 of water, 1 in 50 of alcohol and 1 in 10 of methyl alcohol, but almost insoluble in acetone and ether. The aqueous solution is stable to heat, and may be sterilised by autoclaving.

**Antidote**. Untoward effects may be relieved by the injection of atropine  $\frac{1}{100}$  gr.

**Uses**. Carbachol exerts effects similar to those of acetylcholine, but it is also active orally and has a more persistent action. It stimulates the parasympathetic nervous system, lowers the blood pressure and dilates the peripheral blood vessels. Carbachol causes contraction of the intestinal and bladder muscle, and is used subcutaneously or intramuscularly to relieve post-operative intestinal atony and to promote micturition due to atony of the bladder wall. The action of carbachol by the mouth is less certain than by injection, but good results are said to have been obtained in paroxysmal tachycardia by the oral administration of from  $\frac{1}{8}$  to  $\frac{1}{4}$  gr. It is also used as eye-drops in an 0.75% solution for decreasing intra-ocular pressure in glaucoma, and 10 drops of an 0.05% solution applied intranasally three times a day is of value in ozæna. The solution may also be applied with a brush or spray.

The results of the administration of carbaminoylcholine to man show that it has in general the same actions as acetylcholine, but because of its increased stability it is effective by intramuscular and subcutaneous injections, and these actions can be maintained for a much longer time than is possible with acetylcholine. By oral administration its effects appear to be less certain, and when given repeatedly malaise and headache result. It can be administered slowly over long periods by ionisation, and local effects in the eye can be obtained by conjunctival instillation. Further, in comparison with acetylcholine the effects on the gastro-intestinal tract and the bladder appear to be greater and those on the cardiovascular system less.—F. R. Fraser, *Brit. med. J.*, i/1938, 1293.

Doryl is useful in the relief of post-operative retention of urine. It has less effect in cases with mechanical obstruction, but is still worthy of trial before resorting to catheterisation. Minor side-effects (salivation, sweating, nausea, shivering, faintness, passage of flatus) make its use inadvisable for very ill or shocked patients. It is also suggested that it should be given an extensive trial

in the treatment of urinary retention associated with spinal cord injuries or tumours or diseases.—R. Officer and J. C. Stewart, *Lancet*, ii/1937, 850.

About a dozen cases of urinary retention which would otherwise have needed catheterisation successfully treated by an intramuscular injection of 0.25 mg. of Doryl.—H. Stalker, *Brit. med. J.*, i/1938, 1393.

**Lentin** (*Merck, Darmstadt; Savory & Moore, London*). Carbaminoylcholine chloride for veterinary use.

*Note*.—Formerly the words "LENTIN" and "LENTINE" were applied to *m*-phenylenediamine.

### Acetyl- $\beta$ -methylcholine Chloride.

$(\text{CH}_3)_3\text{NCl}\cdot\text{CH}_2\cdot\text{CH}(\text{CH}_3)\text{O}\cdot\text{CO}\cdot\text{CH}_3=195.72$ . *Prop. Name.* MECHOLYL (*Merck, Darmstadt; Savory & Moore, London*).

*Dose*.—Orally, 3 to  $7\frac{1}{2}$  grains (0.2 to 0.5 g.); subcutaneously, up to 0.025 g. *It should not be given intravenously.*

Acetyl- $\beta$ -methylcholine chloride is a very deliquescent, white, odourless, crystalline substance melting at  $172^\circ$ .

Very *soluble* in water and alcohol, the aqueous solution having a bitter taste and only limited stability.

**Contraindications.** It should not be given to patients who are seriously ill or who have asthma, and should be used with caution in elderly patients.

**Antidote.** Atropine  $\frac{1}{100}$  grain, instantly destroys the action of acetyl- $\beta$ -methylcholine chloride.

**Uses.** The action of acetyl- $\beta$ -methylcholine chloride, whether given by the mouth or by injection, is similar to that of acetylcholine, but it is more stable than the latter and is therefore better suited to clinical use. It is a stimulant of the parasympathetic and antagonises adrenaline. It slows the heart and lowers blood pressure, dilates peripheral blood vessels, increases intestinal tone and peristalsis, and stimulates the activity of the salivary and sweat glands. It has been employed *per os* in a dose of 3 to  $7\frac{1}{2}$  gr. two or three times daily in atony of the bladder and intestinal distension. Subcutaneously it has been employed with success in paroxysmal tachycardia, in post-operative abdominal distension, and in various types of peripheral vascular disease. Subcutaneous injections cause a rapid and sharp fall in blood pressure and a rise in the pulse rate, the action lasting for 15 to 20 minutes. For the treatment of conditions such as Raynaud's disease, varicose ulcers, etc., some workers prefer to employ the substance by ionisation, using a 0.1 to 0.5% aqueous solution, which produces the desired local effects without the pronounced systemic effects caused by injections.

A warning as to confusion with acetylcholine. Given subcutaneously, acetyl- $\beta$ -methylcholine is somewhere between 10 and 20 times as powerful as acetylcholine, and an injection of 75 mg. to a boy of 14 would probably produce enough vagus effect to stop the heart altogether.—I. Starr, *per Lancet*, i/1936, 391.

Like carbaminoylcholine, acetyl- $\beta$ -methylcholine has actions similar to those of acetylcholine and is more stable, producing typical effects when given by subcutaneous or intramuscular injection, by the mouth, or by ionisation. By injection, a dose of 10 to 25 mg. appears to be comparable to 0.25 to 0.5 mg. of carbaminoylcholine. With both esters the results following injection appear in a few minutes, but while the action on the cardiovascular system passes off in from 30 to 40 minutes the action on the gastro-intestinal tract and bladder may persist for several hours. It is generally accepted that the action of



carbaminoylecholine on the gastro-intestinal tract is relatively greater than on the cardiovascular system, and that the reverse is the case with acetyl- $\beta$ -methylcholine.—F. R. Fraser, *Brit. med. J.*, i/1938, 1293.

Acetyl- $\beta$ -methylcholine is rapidly absorbed by the nasal mucous membrane when administered in a glycol or water vehicle. Small doses (25 to 250 mg.) administered by this method produce local and general reactions, the most easily measured of which is a drop in blood pressure.—T. R. Van Dellen, M. Bruger and I. S. Wright, *J. Pharmacol.*, 1937, 59, 379.

In the presence of a very small amount of one of the drugs of the atropine series within the body, acetyl- $\beta$ -methylcholine fails to cause its characteristic effects of perspiration, salivation, lachrymation and rhinorrhœa. Thus it may be used as a diagnostic test for poisoning created by any one of the atropine series of drugs.—W. Domeshek and O. Feinsilver, *J. Amer. med. Ass.*, ii/1937, 561.

**PAROXYSMAL TACHYCARDIA.** The dose should be increased in reference to age, the optimum dose being 10 mg. at the age of 20, increasing to 30 mg. at the age of 60. This is probably related to the weight of the patient. Toxic effects with alarming symptoms may follow intravenous injection. Asthmatic attacks in patients subject to this disease may occur and substernal pain on rare occasions, but there is no evidence to show that the drug is dangerous when administered in the proper dosage and in the proper manner. It is only occasionally successful in auricular flutter.—*Amer. J. med. Sci.*, 1936, 191, 210.

## ACIDUM ACETYLSALICYLICUM

B.P., U.S.P. XI, *Fr. Cx.*, *P. Jap. V.*, etc.

$\text{CH}_3\text{CO}\cdot\text{O}\cdot\text{C}_6\text{H}_4\cdot\text{COOH} = 180.06.$

**Syn. ASPIRIN.** This name is public property in Great Britain and Northern Ireland. In other countries it is a registered trade mark. ASPRO (*Aspro Ltd., Slough*), EMPIRIN (*Burroughs Wellcome, London*), GENASPRIN (*Genatosan, Loughborough*), are further names for the substance in tablet form. ASPIRGRAN (*Monsanto Chemicals Ltd., London*) is a granular form.

**Dose.**—5 to 15 grains (0.3 to 1 g.), in cachets, tablets, or suspended in a good draught of water thrice daily after meals—not on an empty stomach. Children  $\frac{1}{2}$  to 5 grains (0.03 to 0.3 g.). *P. Ital. V* has 3 g. as max. dose in 24 hours; *F.E. VIII*, 5 g.; *Fr. Cx.*, 6 g.

A white crystalline powder, m.p. 135° to 138°. It is not completely stable—all samples have an odour of acetic acid. In dry air it is fairly stable, but in contact with moisture it gradually hydrolyses into salicylic and acetic acids. In solution with alkalis this hydrolysis proceeds rapidly, and the clear solutions formed may consist entirely of acetate and salicylate.

**Soluble** about 1 in 300 of water, 1 in 5 of alcohol 90%, 1 in 17 of chloroform, 1 in 20 of ether.

**Incompatible** with free acids, acetanilide, phenazone, hexamine, acacia, iron salts and alkalis.

**Antidotes.** Empty stomach by emetic, or by stomach tube using 5% sodium bicarbonate solution. Keep patient warm. Give milk or water freely, containing a little sodium bicarbonate. Stimulants if necessary. Saline infusion, with dextrose, if required.

The dangerous dose of aspirin probably varies considerably around 400 to 500 gr., but, in the light of more recent observation on the beneficial results of treatment, lethal effect may be avoided

even when more than 500 gr. are ingested. It seems reasonable to believe that even when the symptoms of poisoning have reached an advanced stage, the combined therapeutic effect of the introduction of fluid to the body and the simultaneous aspiration of cerebrospinal fluid will be the means of saving an otherwise hopeless situation.

**Reports of poisoning.** Notes on four fatal cases and on two cases with recovery following the taking of 500 and 435 gr. respectively.—A. V. Neale, *Brit. med. J.*, i/1936, 110.

Case of woman who took about 435 gr. of acetylsalicylic acid ending in recovery; glucose, 5% in saline, by rectum, and fruit juice with glucose by mouth, were given freely. Strikingly beneficial effect of lumbar puncture.—S. C. Dyke, *Lancet*, ii/1935, 613.

Attempted suicide by taking 600 gr. Recovery without active treatment.—S. Lipetz, *Brit. med. J.*, i/1934, 652.

Attempted suicide from 450 gr. Cyanosis, and later œdema and enlargement of heart. Recovery.—*Lancet*, i/1933, 490.

Two infants of 14 months and 2 years and 8 months developed severe toxic symptoms after ingestion of 30 gr. and 60 gr. respectively. Both recovered following injection of Hartmann's solution intravenously.—S. W. Williams and R. M. Panting, *Brit. med. J.*, i/1937, 550.

Death of a woman, aged 30, after swallowing 100 5-gr. tablets.—E. Biddle, *Brit. med. J.*, i/1938, 1365.

**Toxic Effects.** May occasionally cause gastric pain, vomiting and giddiness, œdema of face and skin rash, even in relatively small doses. It should be administered on a full stomach.

Dyspnoea is an important symptom of salicylate poisoning, and it is largely because of this hyperpnoea that acidosis of diabetic or renal origin is often suspected unless there is a clear history of the ingestion of salicylate. The finding of the violet colour reaction in the spinal fluid with ferric chloride may be a useful differential diagnostic procedure. The following symptoms are rarely seen in diabetic acidosis but frequently in salicylate poisoning: tinnitus, twitching, convulsion, deafness, dimness of vision, sweating, hallucinations, disorientation, delirium and urticaria.—B. D. Bowen, J. F. Ronfa and O. W. Clinger, *J. Amer. med. Ass.*, ii/1936, 276.

The diagnosis of hypersensitivity for aspirin usually may be made easily by simply questioning the patient. Use of skin tests is not advised in patients with a personal or family history of allergic disease, since they will often be negative even though the patient is hypersensitive to the drug, and if positive they may provoke severe reactions. Aspirin should always be employed with caution in the treatment of asthmatic patients, and should never be given to one who has nasal polyps.—H. F. Buchstein and L. E. Prickman, *Proc. Mayo Clin.*, 1937, 616.

From gastroscopic observation it is concluded that acetylsalicylic acid (in the form of aspirin and certain proprietary preparations) is a gastric irritant, and may thus cause indigestion and hæmorrhage, or, if taken repeatedly, chronic gastritis. If taken after food or with milk it probably has no deleterious effect. Calcium acetylsalicylate is less irritating.—A. H. Douthwaite and G. A. M. Lintott, *Lancet*, ii/1938, 1222.

**Uses.** Analgesic and antipyretic. It has anti-rheumatic properties, and is useful in influenza (especially with quinine), acute and chronic affections of the joints, headaches and in gout, neuralgia, chorea, and pleurisy. In influenzal complaints a dose taken at bed-time will often induce perspiration; quiet sleep follows, fever is reduced and pulse improves. In some cases, it is useful with caffeine or with phenacetin and Dover's powder. The latter combination is useful also in measles and mumps. Aspirin gargle (10 gr. to 1 oz. of water) is very useful after tonsillectomy and operations on the pharynx.

Appreciable quantities of the calcium of the teeth go into solution when an aspirin gargle is used, and the use of such a gargle over a number of years might well result in permanent damage to the teeth. The fairly alkaline solution of sodium salicylate obtained by dissolving equal weights of aspirin and sodium bicarbonate has no appreciable effect on the teeth.—D. B. Dott, *Edinb. med. J.*, 1940, 700.

**ACUTE RHEUMATISM.** Aspirin in the same dosage would appear to be equally efficacious, if not more so, than sodium salicylate, in reducing pain and fever, but less frequently produces signs of poisoning, and there would appear to be no need to give alkalis with this drug. Yet it must be remembered that some pharmacologists consider aspirin to be more toxic than sodium salicylate. Clinical experience, however, hardly supports this view, and we have come to regard aspirin as the more useful of the two drugs.—C. Bruce Perry, *Med. Pr.*, 1936, 136.

**Mistura Acidi Acetylsalicylici (B.P.C.).** *Syn.* ASPIRIN MIXTURE.

*Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.).

Acetylsalicylic acid 15 gr. suspended with compound powder of tragacanth in chloroform water to 1 oz.

**Mistura Acidi Acetylsalicylici Composita (B.P.C.).** *Syn.* COMPOUND ASPIRIN MIXTURE.

*Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.).

Acetylsalicylic acid 15 gr., dissolved with the aid of potassium citrate 30 gr., in syrup of lemon and chloroform water to 1 oz.

**Mist. Acid. Acetylsal. (N.I.F.).**

Acetylsalicylic acid 7½ gr., potassium citrate 15 gr., chloroform water to ½ oz.

**Hauftus Acidi Acetylsalicylici Compositus (Mid. H.).**

Acetylsalicylic acid 5 gr., phenacetin 5 gr., caffeine citrate 2½ gr., compound powder of tragacanth 10 gr., chloroform water to 1 oz.

[P1] **Mistura Acidi Acetylsalicylici Composita (W.H.).**

*Syn.* MORGAN'S MIXTURE.

Acetylsalicylic acid 5 gr., caffeine citrate 2 gr., potassium citrate 20 gr., camphorated tincture of opium 15 m., liquid extract of liquorice 15 m., chloroform water to ½ oz.

Acetylsalicylic acid (3%) dissolved in alcohol 50% loses about 1.5% per day, 6.0 to 6.5% per week and 13.5 to 14.5% per month. A suspension of the same strength, and kept under the same conditions, loses 0.3% per day, 1.6 to 2.0% per week and 7 to 8% per month. Suspensions should be prescribed and dispensed in preference to solutions containing ammonium acetate or similar substances, and where administrations of tablets is not desired.—H. W. Tomski and L. J. Waller, *Pharm. J.*, i/1940, 53.

**Tabellæ Acidi Acetylsalicylici (B.P.C.)** contain 5 gr. (0.3 g.).

**Tabellæ Acidi Acetylsalicylici et Caffeinæ (B.P.C.)** contain acetylsalicylic acid 4 gr. and caffeine 1 gr.

**Tabellæ Acidi Acetylsalicylici Compositæ (B.P.C.).** *Syn.* TAB. ASPIRIN. Co. (N.I.F.), COMPOUND ASPIRIN TABLETS. Contain acetylsalicylic acid 3½ gr., phenacetin 2½ gr. and caffeine ½ gr.

[P1-81] **Tabellæ Acidi Acetylsalicylici et Opii (B.P.C.).** *Syn.* TAB. ASPIRIN. ET DOVER. (N.I.F.), TABLETS OF ASPIRIN AND DOVER'S POWDER.

Contain acetylsalicylic acid 2½ gr. and powder of ipecacuanha and opium 2½ gr. (*Exempt* [D].)

[P1] **Tabellæ Acidi Acetylsalicylici et Opii Compositæ**  
(*B.P.C.*). *Syn.* TAB. ASPIRIN. ET DOVER. CO. (*N.I.F.*).

Contain acetylsalicylic acid 3 gr., phenacetin  $1\frac{1}{2}$  gr., and powder of ipecacuanha and opium 1 gr.

[P1-S1] **Pilula Aspirin et Acidi Arseniosi (Hoedemaker's Pill)** (*Vic. Park*).

Aspirin  $2\frac{1}{2}$  gr., arsenic trioxide  $\frac{1}{2}$  gr., starch and distilled water sufficient to make into 100 pills. *Dose.*—2 pills thrice daily, increasing carefully by one pill every second day to a maximum, continued for a period, of never more than 25 pills daily, and then reducing at the same rate.

**Albyl Tablets** (*Bencard, London*). Peppermint-flavoured tablets containing acetylsalicylic acid 5 gr., heavy magnesium oxide 0.8 gr. Stated to be less irritating to the mucous membrane of the stomach.

**Anadin** (*Anadin, London*). Tablets containing in each: aspirin 3 gr., phenacetin 3 gr., caffeine  $\frac{1}{2}$  gr., quinine sulphate  $\frac{1}{2}$  gr.

**Arifphon** (*Lilly, London*). Aspirin  $2\frac{1}{2}$  gr., sodium citrate 5 gr., caffeine citrate  $\frac{1}{2}$  gr., in capsules.

**Aspiphnenin** (*Bayr Products, London*). Tablets containing aspirin 5 gr., phenacetin  $2\frac{1}{2}$  gr.

**Bromalgin** (*Reynolds & Branson, Leeds*). Contains aspirin, caffeine citrate and potassium bromide. *Dose.*—1 or 2 drachms, well diluted. A general analgesic.

**Caffacetin** (*Duncan, Flockhart, Edinburgh*). Tablets containing  $2\frac{1}{2}$  gr. each of phenacetin, aspirin and caffeine citrate.

**Collopyrin** (*Crookes Laboratories, London*). Acetylsalicylic acid 5 gr. with kaolin. *Dose.*—1 or 2 tablets three or four times daily.

**Emocin** (*Burroughs Wellcome, London*). Lozenges containing acetylsalicylic acid 2 gr., in a flavoured demulcent base. For sore throats.

[P1] **Fibrosan** (*John Wyeth, London*). Tablets each containing acetylsalicylic acid 2 gr., salol 1 gr., sodium salicylate 2 gr., strychnine sulphate  $\frac{1}{100}$  gr., calcium carbonate 1 gr. *Dose.*—2 tablets thrice daily. Advocated for the relief of pain in rheumatic affections, influenza, dysmenorrhœa and migraine.

**Calcii Acetylsalicylas** (*B.P.C., P. Ned. V Supp II*).

*Prop. Names.* KALMOPYRIN (*Richter, London*), TYLCALSIN (*Martindale, London*).  $(\text{CH}_3\text{CO}\cdot\text{OC}_6\text{H}_4\cdot\text{COO})_2\text{Ca}\cdot 2\text{H}_2\text{O} = 434.2$ .

*Dose.*—5 to 15 grains (0.3 to 1 g.), in cachets or tablets, followed by a draught of water.

White amorphous non-hygroscopic powder, decomposing in moist air. It may be prepared in a stabilised form containing from 5 to 7% of calcium chloride by adding sodium bicarbonate to a suspension of finely powdered acetylsalicylic acid in a solution of calcium chloride, stirring until effervescence ceases, filtering, washing the precipitated product with a solution of calcium chloride and drying *in vacuo*. The increased stability appears to be due to the removal of the water of crystallisation and of absorbed moisture by the calcium chloride, thereby retarding hydrolysis. In aqueous solution, the stabilised salt becomes hydrolysed as rapidly as the unstabilised salt, with the formation of calcium salicylate and acetic acid. Stabilised calcium acetylsalicylate is an odourless, tasteless, white powder.

**Soluble** 1 in 5 of water; slightly soluble in alcohol.

**Uses.** In view of its greater solubility, calcium acetylsalicylate forms a useful alternative to aspirin. It is more readily absorbed, is often better tolerated and causes less gastric irritation.

A prompt rheumatic and influenza specific, also in catarrhs and neuralgia and for relief of pain. In lumbago 2 tablets at night in

hot tea (as diaphoretic) valuable. In gonorrhœal rheumatism has given excellent results.

Considerably less toxic than ordinary aspirin and much larger doses can safely be used when required. It is not contraindicated in cases of cardiac weakness and is especially suitable in conditions known to be unfavourably sensitive to ordinary salicylate medication. It is analgesic, antipyretic, diaphoretic, sedative and antirheumatic, and is markedly superior to ordinary aspirin in the treatment of chorea in children; it is also a good source of easily assimilable calcium (10%) and is of value for women during pregnancy and lactation, for growing children, senile cases and in arthritic patients where salicylate therapy is indicated.—M. Coplans, *Med. Pr.*, ii/1939, 199.

**CHOREA.** Satisfactory clinical results—with an average daily dose *per os* of from 30 to 45 gr. of calcium aspirin for a child of 12. It has a triple action: (1) antirheumatic, (2) correction of Ca deficiency, (3) sedative to brain.—N. Mutch, *Brit. med. J.*, ii/1934, 248. See also N. Hill, *Med. Pr.*, 1936, 415.

Treatment with calcium aspirin gives good clinical results in Sydenham's chorea and considerably shortens the duration of the disease, but it is simply symptomatic. The calcium probably acts as a nerve sedative and the salicylates have a beneficial effect on the rheumatic infection.—G. E. G. Pearson, *Canad. med. Ass. J.*, i/1937, 576.

### Calcium Acetylsalicylate Intravenously.

**Dose.**—The usual dose is 0.5 g. in 10 to 20 ml. of sterile water, but larger doses, even 2 g., have been injected *very slowly*. Solutions must not be heated. The concentration is of importance; it should not exceed 5%.

**Uses.** Successful in sciatica, acute rheumatism, tabes dorsalis, interstitial keratitis, acute iritis, gonorrhœal synovitis, dysmenorrhœa and severe headaches of doubtful causation. Psoriasis of 15 years standing was treated by the method with marvellous result; the affection cleared up completely. Of considerable value in rheumatic endocarditis. 0.25 g. has been given to children of 14.

In acute and subacute rheumatism and in septicæmia useful intravenously.—H. Pritchard, *Brit. med. J.*, i/1927, 794.

Rapid results in rheumatic infections from Tylcalsin intravenously.—J. Burnford, *Lancet*, i/1931, 351.

**Alasil Tablets (Wander, London).** **Dose.**—1 or 2 thrice daily in an ample supply of water. Tablets containing calcium acetylsalicylate 7½ gr. and Alocol (colloidal aluminium hydroxide) 6 gr. Antipyretic, analgesic and sedative. In rheumatic affections, influenza, chills, neuralgia and cough.

**Caleno (J. C. Eno, London).** Calcium acetylsalicylate stabilised by the addition of up to 5% of calcium chloride. Issued in powder form only.

**Kafalgol (Richter, London).** Calcium acetylsalicylate 0.5 g., caffeine 0.05 g. **Dose.**—2 to 3 tablets daily. In headache, toothache, etc.

**Lithii Acetylsalicylas (B.P.C.).**  $\text{CH}_3\text{CO}\cdot\text{OC}_6\text{H}_4\cdot\text{COOLi}$  = 186.0. **Prop. Names.** HYDROFYRIN (Richter, London), LITMOFYRINE (A. Bishop Ltd., London), TYLLITHIN (Martindale, London).

**Dose.**—5 to 15 grains (0.3 to 1 g.). Maximum daily dose 75 grains. White powder with a bitter taste.

**Soluble** 1 in 1 of water, 1 in 4 of alcohol 90%, insoluble in ether. The salt is to be kept in a well-closed bottle as it undergoes decomposition in moist air.

**Incompatible** with iron salts, mineral acids and alkalis. It is preferably given as cachets or tablets, the latter to be crushed and taken in a little water. It is *not desirable* to give it in mixture form.

**Uses.** Analogous to those of the calcium salt.

**Enema Sedativum (St. G.H.).**

Sodium bromide 1 dr., lithium acetylsalicylate 10 gr., water to 5 oz. To be mixed with an equal quantity of warm water and given immediately after operation.

**Magnesii Acetylsalicylas.** *Prop. Names.* MAGASPIRIN (*Duncan, Flockhart, Edinburgh*), MAGISAL (*Martindale, London*).  
 $(\text{CH}_3\text{CO}\cdot\text{O}\cdot\text{C}_6\text{H}_4\cdot\text{COO})_2\text{Mg}=382\cdot3$ .

*Dose.*—5 to 15 grains (0·3 to 1 g.).

Microcrystalline powder, non-hygroscopic, almost tasteless and odourless, soluble 1 in 12 of water, less readily in alcohol.

**Incompatibility and Uses** are similar to those of the lithium and calcium salts.

**Magsyn** (*Allen & Hanburys, London*). Tablets containing  $7\frac{1}{2}$  gr. of basic magnesium acetylsalicylate. *Dose.*—1 to 3 tablets.

**Sodii Acetylsalicylas.**  $\text{CH}_3\text{CO}\cdot\text{O}\cdot\text{C}_6\text{H}_4\cdot\text{COO}\cdot\text{Na}=202\cdot1$ .

*Dose.*—5 to 15 grains (0·3 to 1 g.).

White amorphous hygroscopic powder, very soluble in water.

*Uses.* Analogous to those of the calcium salt.

**Saligenin.**  $\text{C}_6\text{H}_4\text{CH}_2\text{OH}\cdot\text{OH}=124\cdot1$ . *Dose.*—10 grains (0·6 g.).

This is the alcohol of which salicylic acid is the corresponding acid. It is converted into the acid in the body.

It is formed with glucose on the hydrolysis of salicin. In acute rheumatism it has been well spoken of by R. Stockman.

**Aspirodine** (*Martindale, London*). Acetyliodosalicylic acid, a stable iodine derivative of acetylsalicylic acid containing about 41% of I. For rheumatic affections and arteriosclerosis. *Dose.*—5 grains (0·3 g.) per day after food, preferably given alone; may be increased if required. Cachets, capsules and tablets are available.

**Methyl-Aspirodine** (*Martindale, London*). Methyl acetyliodosalicylate, the methyl ester of Aspirodine. It occurs as white crystals agglomerated into granules, m.p.  $40^\circ$ , containing 39·7% of I. Applied by inunction, it is a prompt local analgesic in rheumatism, neuritis, sciatica, lumbago and other painful affections. Should not be rubbed vigorously into extensive areas unless diluted. **Methyl-Aspirodine Balm** contains 50% of Methyl-Aspirodine in a lanolin base. **Methyl-Aspirodine Liniment** contains 25% of Methyl-Aspirodine with camphor, chloroform and menthol.

**Phenyl-Aspirodine** (*Martindale, London*). Acetyliodosalol, for use as an intestinal and urinary antiseptic. *Dose.*—5 grains (0·3 g.), administered alone as a cachet, capsule or tablet, in water.

**Sedaspurin** (*Martindale, London*). Acetyl bromosalicylic acid, a stable compound containing approximately 31% of Br. It combines the analgesic and antipyretic properties of aspirin with the sedative action of the bromides. For use in headache, dysmenorrhœa, insomnia, tonsillitis, etc. *Dose.*—5 to 10 grains (0·3 to 0·6 g.), preferably given alone as a cachet, capsule or tablet.

### **Ammonium Ortho-iodoxybenzoate.**

*Syn.* AMIODOXYL BENZOATE.  $\text{C}_6\text{H}_4(\text{IO}_2)\cdot\text{COONH}_4=297\cdot0$ .

A white crystalline powder containing 42·7% of I, readily soluble in water. To avoid decomposition it should be kept dry and away from sunlight. *Dose.*—11 to 15 grains (0·75 to 1 g.) intravenously, or twice this dose orally.

**Uses.** Chiefly in arthritis, especially active infection. It is given in 100 ml. of normal saline intravenously within 7 to 12 minutes, but orally and in 2 g. doses by high enema it has been found effective. Following intravenous use, reactions resembling non-specific protein reactions may occur. The salt is quickly reduced in the blood stream, and it is stated to stimulate phagocytosis of streptococci and staphylococci.

**Arthrytin** (*Pharmaceutical Specialities (May & Baker) Ltd., London*). Calcium o-iodoxybenzoate. Tablets contain 0·5 g. *Dose.*—1 tablet with a glassful of water thrice daily after meals. Treatment should be continued for a number of months. For the hypertrophic and atrophic types of arthritis.

Good results have also been obtained in leg ulcer. The ammonium salt is also available for intravenous use. Oral administration of the calcium salt is stated not to be followed by the reactions associated with intravenous administration of the ammonium salt.

**Calsiod** (Smith, Kline & French, Philadelphia; Menley & James, London). Calcium *o*-iodoxybenzoate. Tablets contain 0.5 g. Arthritis and rheumatic conditions.

**Acetyl-para-amidosalol.**  $C_6H_4OH \cdot COO \cdot C_6H_4NH \cdot COCH_3 = 271.16$ .  
*Prop. Name.* SALOPHEN (Bayer Products, London). (P. Belg., P. Helv. V, P. Ned. V, Fr. Cx., F.E. VIII, P. Ital. V, P. Svec).

*Dose.*—5 to 15 grains (0.3 to 1 g.) 3 or 4 times a day in cachets.

White crystalline scales, tasteless; soluble 1 in 160 of alcohol, 1 in 105 of chloroform, ether, and alkalis, almost insoluble in water. It contains about 50% salicylic acid.

**Incompatible** with alkalis and their carbonates, and with hexamine. It is unaffected by gastric juice, but decomposed by pancreatic ferment.

**Uses.** Febrifuge and anti-rheumatic. Used in chorea, neuralgia, sciatica, headache and throat affections. Ointment 10% in lanolin for psoriasis and other skin affections.

## ACIDUM ASCORBICUM

(with VITAMIN K, etc.)

*B.P. Add. I, U.S.P. XI Supp. II, Fr. Cx., etc.*



*Syn. and Prop. Names,* VITAMIN C, CEVITAMIC ACID, REDOXON (Roche Products, Welwyn Garden City), CANTAN (Bayer Products, London), CELIN (Glaxo Laboratories, London), DAVITAMON C (Organon Laboratories, London), PLANAVIT C (Pharmaceutical Specialities (May & Baker) Ltd., London).

*Dose.*—Prophylactic (daily),  $\frac{2}{3}$  to  $\frac{4}{5}$  grain (0.025 to 0.05 g.), equivalent to 500 to 1000 units. Therapeutic (daily),  $1\frac{1}{2}$  to 4 grains (0.1 to 0.25 g.), equivalent to 2000 to 5000 units. *U.S.P. XI Supp. II* has average daily dose  $\frac{3}{4}$  grain (0.05 g.), equivalent to 1000 units.

In colourless, odourless crystals with an acid taste. It is obtained synthetically or may be extracted from the ripe fruit of *Capsicum annuum* or from other vegetable sources. Chemically ascorbic acid is the enolic form of 3-keto-*l*-gulofuranolactone. It contains 20,000 units per g.

**Soluble** 1 in 3 of water, 1 in about 30 of alcohol 95%; less soluble in methyl alcohol and acetone; insoluble in chloroform, benzene, ether and light petroleum. Ascorbic acid in alkaline solution (pH 8.3) can be sterilised by heating at 100° for one hour.

**Human Requirements.** The minimum daily requirement of ascorbic acid for an adult is about 25 mg. The requirements of infants and children are proportionately greater than those of adults, and it would appear that infants should receive at least one-third as much ascorbic acid, calculated per unit of body weight, as adults. Thus the minimum level for infants should be not less than 10 mg.

These quantities are normally supplied in the diet, but individuals vary greatly in their requirements, and the higher the

metabolism (as in pregnancy and lactation) the greater is the need, and for prophylactic purposes doses of at least double the minimum requirements are therefore advised, while in cases of known deficiency, or where there is excessive excretion, doses of 100 to 300 mg. are employed.

**Uses.** Ascorbic acid regulates the oxidation-reduction processes of the living cell. It plays an important part in connection with resistance to bacterial infection and toxins, and acts as a general cell stimulant and detoxicating agent in infections. Clinical scurvy, which is the outcome of severe ascorbic acid deficiency, is seldom seen now in adults but is still a not uncommon disease in infants, and an ample intake of ascorbic acid is therefore a matter of major importance during pregnancy and lactation. It is now generally agreed, moreover, that a minor degree of ascorbic acid deficiency, which has been termed "latent scurvy," is relatively common among adults and is the cause of much ill-health.

In addition to its use as a specific in the prophylaxis and treatment of scurvy, ascorbic acid has been employed with varying success in the treatment of numerous other diseases. These may be classified as (a) those diseases which are due, in greater or less degree, to an initial deficiency of ascorbic acid, and (b) those diseases in which, owing to increased excretion, the normal ascorbic acid requirements are augmented. Among the former may be mentioned (apart from scurvy) anæmia, and especially the anæmias of childhood, increased capillary fragility, hæmophilia, dental caries, gingivitis and cataract, and among the latter the infectious diseases such as influenza, whooping cough, diphtheria, rheumatic fever, and pneumonia.

Ascorbic acid should also be used as a prophylactic measure in gastric and duodenal ulcer when restricted diets are prescribed.

It seems justifiable for the clinician to assume that orange juice contains about 50 mg. of ascorbic acid per 100 ml., tomato juice 17 mg., and pineapple juice 10 mg. In his approximation of prophylactic doses he can consider 50 ml. of orange juice (containing 25 mg. of ascorbic acid) as a nutritional unit, equivalent to 150 ml. of tomato juice and 250 ml. of pineapple juice. The effect of usual home procedures can be ignored although storage for more than two days, even in the refrigerator, has a progressively destructive effect on the vitamin.—T. H. Ingalls, *New Engl. J. Med.*, ii/1939, 685.

**ARSENICAL DERMATITIS.** Toxic effects after the arsenical anti-syphilitic drugs may be counteracted by ascorbic acid, which appears to have a pronounced detoxicating influence and has a beneficial effect on dermatitis following nearsphenamine. For cases of exfoliative dermatitis the daily subcutaneous injection of 1 ml. of 5% solution, with two tablets of 50 mg. thrice daily, is advised.—R. Lees, *Practitioner*, ii/1937, 418.

**CATARACT.** A case of bilateral cataract following treatment with dinitrophenol. The right eye was treated surgically, but when the left cataract was ready for extraction vitamin C was administered orally, 40 fl. oz. of orange juice and subsequently 500 mg. of the synthetic vitamin in addition being given daily. Definite improvement occurred.—S. Simkins, *J. Amer. med. Ass.*, i/1937, 2193.

**DERMATITIS.** Striking effect of L-ascorbic acid (vitamin C) on five cases—three of dermatitis produced by arsenobenzene, a case of intolerance to the drug, and a case of gold dermatitis. The good effects of the injections were almost immediately noticeable, and a cure effected in two or three weeks in cases which might have persisted for months or have had even a fatal issue. 0.05 g. was given intravenously dissolved in distilled water. In one patient whose dermatitis made it impossible



to find a vein, the drug was given orally three times a day with equally good results.—I. Dainow, per *Brit. J. Derm.*, 1936, 48, 167.

**HÆMORRHAGE.** Five cases of capillary hæmorrhage (essential thrombopenia, purpura infectiosa, essential hæmaturia) satisfactorily treated by intravenous injections of from 100 to 200 mg. daily. Should not attempt treatment in venous or arterial hæmorrhage.—H. Engelkes, *Lancet*, ii/1935, 1285.

A case of hæmorrhage in the right eye recurring at intervals of about 20 days and treated by oral administration of vitamin C as a proprietary preparation, Redoxon, cleared up quickly and there was no further remission during several months.—H. Villard and co-workers, per *Nutr. Abstr. Rev.*, Jan., 1936, 744.

**HEART FAILURE.** Vitamin C increased the urinary output in each of 8 patients with heart failure and in another with considerable œdema of the lower extremities of unknown origin. In 2 patients the increase was slight, in 4 it was either moderate or considerable, and in 3 cases it was great. These results indicate the need of providing an adequate supply of vitamin C for all patients with heart failure.—W. Evans, *Lancet*, i/1938, 308.

**PAROXYSMAL HÆMOGLOBINURIA** successfully treated with ascorbic acid, 300 mg. intravenously for several days. The hæmoglobinuria disappeared, and although treatment has now been stopped for 6 weeks paroxysms (due to cold) cannot now be stimulated. Suggested trial in blackwater fever.—L. Armentano, *Nature, Lond.*, i/1936, 910.

**PEPTIC ULCER.** Diets given to patients with peptic ulcer are generally deficient in vitamin C, and the deficiency may play an important part in the ætiology of hæmorrhagic gastro-duodenal lesions. Ascorbic acid should be administered to ulcer patients, particularly when there is a tendency to hæmorrhage.—A. B. Rivers and L. A. Carlson, *Proc. Mayo Clin.*, 1937, 383.

The amount of ascorbic acid in the blood plasma was determined in 20 patients with gastric or duodenal ulcers, and 18 of them were found to have low values. In most of the cases it could be demonstrated that the patients had actually taken an inadequate amount of vitamin C, and there is evidence that if a sufficient amount of the vitamin is ingested the blood values can be raised to normal. It is important for the physician to make sure that patients with peptic ulcer are receiving an adequate amount of vitamin C.—T. H. Ingalls and H. A. Warren, *New Engl. J. Med.*, ii/1937, 443.

It was found that 5 patients with duodenal ulcer utilised 20% more ascorbic acid than normal individuals. It was found that these patients had been taking diets deficient in vitamin C. The usual Sippy diet contains much less than the normal requirements of vitamin C. This deficiency can be remedied by including in the daily diet juice of one or two good-sized oranges.—H. A. Warren *et al.*, *New Engl. J. Med.*, i/1939, 1062.

**PNEUMONIA.** Sixteen patients suffering from fibrinous pneumonia were treated with ascorbic acid. During the first few days 400 or 500 mg. was injected three times daily intramuscularly until the temperature had fallen to normal or the appearance of ascorbic acid in the urine showed that the saturation point had been reached. Then, and until recovery, 100 mg. of ascorbic acid was given three times daily by the mouth, employing the sodium salt of *L*-ascorbic acid. Other treatment was limited to expectorants and drugs with an action on the cardiovascular system. Even after the first injection there was often an encouraging response, indicated by an improvement in the respiration and in the patient's symptoms, and it was remarkable that all the 16 cases yielded little or no sputum. The fall of temperature in 8 cases was by crisis.—E. Bohnholtzer, *Dtsch. med. Wschr.*, i/1937, 1001.

**RHEUMATISM, JUVENILE.** A group of 64 controls excreted more ascorbic acid than the standard amount of 13 mg. per day per 10 st. of body weight, the average being 20 mg. A group of 107 active rheumatic cases, receiving the same institutional diets for periods of up to several months, excreted an average of only 9 mg. per day per 10 st. of body weight. A group of 23 cases of active surgical tuberculosis also showed a low rate of excretion, in common with other infections or pyrexial conditions. Cases of quiescent tuberculosis gave normal rates. It is suggested that in the infection which underlies rheumatic fever there is a greatly increased metabolic use of (and need for) vitamin C. In the absence of generally accepted medical teaching in the matter, further clinical trial of vitamin C therapy in rheumatic fever is suggested.—M. A. Abbasy *et al.*, *Lancet*, ii/1936, 1413.

**RHEUMATOID ARTHRITIS.** Definite clinical improvement in 5 out of 6 cases on a high vitamin C diet.—D. C. Hare and E. C. P. Williams, *Lancet*, i/1938, 20.

**SCURVY.** A case of scurvy accompanied by a condition of gastric achylia subsequent to alcoholic gastritis was cured by a daily intravenous injection of 40 mg. of ascorbic acid, the diet being kept the same during the time of the injections as it was before.—Schultzer, *Lancet*, ii/1933, 589.

30 mg. ascorbic acid daily given by mouth completely cured infantile scurvy in 2 children in 1 to 2 weeks.—E. Svensgaard, *Lancet*, i/1934, 22.

A mild case in a child, 9 months old, successfully treated with ascorbic acid. 20 mg. of ascorbic acid dissolved in 2 fl. oz. of water with milk and maltodextrin was given twice daily for 18 days. Dose then reduced to 10 mg. twice daily for 13 days when symptoms cleared up.—L. G. Parsons, *Proc. Roy. Soc. Med.*, 1933, 36, 1534.

A special number (Sir Thomas Barlow Birthday Number) devoted to infantile scurvy—history, ætiology, recognition, effect on tooth structure, treatment, etc.—*Arch. Dis. Childh.*, 1935, 211.

Scurvy and carditis.—S. Taylor, *Lancet*, i/1937, 973.

**TUBERCULOSIS.** Ascorbic acid is of no value in the treatment of pulmonary tuberculosis and its complications, including hæmoptysis. Saturation with the vitamin neither contributes to recovery nor retards retrogression.—G. S. Erwin, *et al.*, *Brit. med. J.*, i/1940, 688.

**WHOOPIING COUGH.** Chemical examination of the urine shows varying degrees of hypovitaminosis-C in whooping cough. Saturation of whooping cough patients with ascorbic acid markedly decreases the intensity, number, and duration of the characteristic symptoms. The routine daily dosage given in divided doses throughout the day now adopted irrespective of age or weight of patient is 350, 250, 250, 200, 200, 150, 150, 125, 125, and 100 mg., continuing at the 100 mg. level until the case is complete, or stopping the dose at any stage at which there was complete remission of symptoms for 2 days. The average total dose is 2700 mg. Where whoop develops during the treatment the dosage may be slightly increased for a few days if desired, but the whoop is mild and soon disappears under the routine treatment.—M. J. Ormerod, B. M. Unkauf, and F. D. White, *Canad. med. Ass. J.*, ii/1937, 268.

If relatively large doses are used early in the disease (e.g., from 150 to 500 mg. daily) the paroxysmal stage is shortened from a matter of weeks to a matter of days. The danger of overdosage seems negligible.—J. M. Ormerod and B. M. Unkauf, *Canad. med. Ass. J.*, ii/1937, 134.

From controlled clinical experiments it is considered that the statement that the administration of vitamin C in whooping cough has an effect upon the course of the disease is at present unproven.—D. Gairdner, *Brit. med. J.*, ii/1938, 742.

**Monoethanolamine Salt of Ascorbic Acid.** In some patients the parenteral administration of ascorbic acid is a necessity and intravenous administration has been widely used but this is associated with considerable loss of vitamin C through the kidneys. On the other hand intramuscular injection of the strong acid causes sloughing of the tissues. The intramuscular injection of the monoethanolamine salt of ascorbic acid presents a simple and effective way of administering vitamin C parenterally. The injections do not give rise to either immediate or delayed local or systemic reactions. The injections are followed by a prompt increase in the vitamin C of the blood. The loss of vitamin C in the urine is not so marked as when ascorbic acid is given intravenously. A patient with marked vitamin C deprivation was saturated in 8 days by the daily intramuscular injection of 100 mg. of the monoethanolamine salt of ascorbic acid.—E. L. Lozner, *New Engl. J. Med.*, i/1939, 987.

**Ceetamin Tablets (Bencard, London).** Tablets prepared from rose hips and containing in each tablet 10 mg. of l-ascorbic acid, together with vitamin C<sub>1</sub> (J factor) and vitamin P.

**Fructamin (Paines & Byrne, London).** Vitamins C and P in powder, tablets and ampoules. Tablets contain 15 mg. of vitamin C complex (=300 i.u. vitamin C). Dose.—1 or 2 tablets three times daily. Ampoules contain 40 mg. of vitamin C complex (=800 i.u. vitamin C) in 1 ml. Dose.—1 or 2 ml. daily intramuscularly or intravenously.

For further particulars of the chemistry of ascorbic acid, see Vol. II.

**Vitamin K.** Vitamin K is widely distributed in nature. In plants its occurrence is almost entirely confined to those structures concerned with photosynthesis. It is present in alfalfa, spinach and sprouting oats. It also occurs in soya-bean oil and some other vegetable oils, but not in fish-liver oils. Vitamin K can be prepared from fish meal, rice bran or casein, if extracts of these materials are allowed to putrefy.

There is evidence that several substances possess Vitamin K activity. That obtained from alfalfa has the empirical formula  $C_{31}H_{46}O_2$  and has been given the name Vitamin  $K_1$  or alpha-phyloquinone; it is 2-methyl-3-phytyl-1:4-naphthoquinone. It is a yellow oil and has been synthesised, the biological activity of the product of the synthesis being identical with that of the natural substance obtained from alfalfa. Another compound with vitamin K activity is obtained from sardine meal. It is possibly 2:3-difarnesyl-1:4-naphthoquinone, and has been termed vitamin  $K_2$ .

Vitamin  $K_2$  has been isolated from a light petroleum extract of purified fish meal, by repeated adsorption followed by crystallisation, in the form of light yellow plates, m.p.  $52^\circ$  to  $53.5^\circ$ .—E. A. Doisy *et al.*, *J. Biol. chem.*, 1939, **131**, 327.

In addition to the vitamins  $K_1$  and  $K_2$ , two other substances exhibiting vitamin K activity are known. The first of these is 2-methyl-3-hydroxy-1:4-naphthoquinone, which has been isolated from *Mycobacterium tuberculosis* and is now prepared synthetically. This substance has been termed phthiocol, but has lower activity than vitamin  $K_1$ . The second substance is 2-methyl-1:4-naphthoquinone (*q.v.*), which appears to exert an activity equivalent to that of vitamin  $K_1$ , but since it is more readily obtained, is likely to replace the latter in clinical use.

**Uses.** Vitamin K was first recognised in 1935 from the fact that chickens fed on a diet deficient in this vitamin developed hæmorrhages, due apparently to a fall in the concentration of prothrombin in the blood resulting in a delayed coagulation time. It is now believed that vitamin K is essential to the normal synthesis of prothrombin in the body and that the liver plays a very important part in this synthesis. Ordinarily most animals obtain sufficient vitamin K from their food or from the products of bacterial metabolism in their intestines, but if there is an inadequate intake of the vitamin in the diet, or if its absorption is impaired owing to an inadequate secretion of bile, or if hepatic damage interferes with the synthesis of prothrombin in spite of an adequate intake of vitamin K, the blood content of prothrombin falls to a low level, resulting in an enormous increase in the clotting time of the blood, so that spontaneous hæmorrhage is likely to occur at the slightest injury. There is at present no method of measuring directly the amount of prothrombin in the blood in order to enable a diagnosis of vitamin K deficiency to be made, or to assess the results of vitamin K therapy, but a fairly accurate determination of the prothrombin level in the blood may be made by Quick's method (*see Vol. II*). Alternatively, a simple bedside test consists in mixing thromboplastin (a saline extract of lung)

with whole blood and observing the clotting time; this is normally from 25 to 30 seconds, but is typically prolonged when the prothrombin level is low.

The chief indications at present for the use of vitamin K are the hæmorrhage associated with obstructive jaundice and hæmorrhagic disease of the newly-born. It is of no value in hæmophilia, purpura and intrinsic diseases of the blood-forming organs or as a non-specific hæmostatic. As a prophylactic its use is indicated in expectant mothers shortly before delivery, in cases of intestinal obstruction, surgical short circuits of the intestines and in the pre-operative and post-operative treatment of cases with obstruction of the common bile duct. Vitamin K may be given orally, in conjunction with bile salts (2 to 4 g.) or, in urgent cases, by duodenal tube; it has also been successfully employed intravenously and intramuscularly.

Vitamin K was employed clinically in 18 cases of obstructive jaundice; in most of the cases there was complete biliary obstruction and subsequent damage to the liver. It was given orally in capsules of 200 mg. daily together with human bile (75 to 150 ml. before each meal) or large doses of bile salts (1000 to 4000 mg.). The results indicated that this treatment reduced elevated prothrombin times to within normal limits and in certain cases probably prevented hæmorrhage or had a definite inhibitory effect on actual bleeding. The results so far obtained encourage the belief that the prevention and control of the hæmorrhagic diathesis of the jaundiced patient may be attained in the not too distant future.—H. R. Butt, A. M. Snell and A. E. Osterberg, *Proc. Mayo Clin.*, 1938, 74.

Apparently vitamin K concentrate will consistently lower the clotting time of the blood in the first few days of life and maintain it at a common lower level.—W. W. Waddell and D. Guerry, *J. Amer. med. Ass.*, 1/1939, 2259.

In normal infants a moderate vitamin K lack develops during the first few days after birth and disappears within a week. This results in a hypoprothrombinæmia which is the cause of the commonly seen slight hæmorrhagic diathesis in the newborn. Its cause must be insufficient supply of vitamin K from the intestine. In diseases belonging to the triad of icterus gravis neonatorum, anæmia neonatorum and hydrops congenitus a very considerable hypoprothrombinæmia has been demonstrated. Ingestion of vitamin K (together with bile salt) by one of the patients resulted in a rapid increase in prothrombin.—H. Dam *et al.*, *Lancet*, ii/1939, 1157.

In 4 patients each presenting a history and physical signs of dietary deficiency disease unassociated with jaundice the prothrombin-time was found to be prolonged. Oral administration of vitamin K without bile salts was followed by a prompt return of the prothrombin-time to normal. It appears that there may be a dietary deficiency of vitamin K in man.—R. Kark and E. L. Lozner, *Lancet*, ii/1939, 1162.

**Klotogen** (Abbott, London). A concentrate rich in vitamin K issued in capsules each containing 1000 Almquist-Stokstad units, and as an oily solution containing 1250 units per ml. *Dose*.—1 capsule three times daily with meals; solution 8 ml. by duodenal tube. It should be used in conjunction with bile salts.

**Methylnaphthoquinone.**  $C_{11}H_8O_2 = 172.2$ . *Prop. Names.* KAPILON (Glaxo Laboratories, London); PROKAYVIT (British Drug Houses, London); (1 ml. ampoules containing 5 mg.).

*Dose*.—5 mg. orally (with 2 or 3 g. of bile salts) or by intramuscular or subcutaneous injection.

1-Methyl-2:4-naphthoquinone is prepared by the oxidation of methyl-naphthalene. It is a lemon-yellow powder with a faint characteristic odour. M.p.  $106^\circ$ . It should be stored in amber coloured bottles.

**Uses.** Analogous to those of vitamin K.

When employed intramuscularly in 4 cases of obstructive jaundice with low prothrombin indices it raised the index considerably in all of them within two days. Its value in the prevention and treatment of hæmorrhage in jaundice is apparent.—J. M. Macfie, A. L. Bacharach and M. R. A. Chance, *Brit. med. J.*, ii/1939, 1220.

The administration of a vitamin K analogue either to the mother between 12 and 4 hours before delivery or to the newborn infant would appear to be specially indicated (1) in cases of maternal toxæmia; (2) in premature labour; (3) in cases of difficult or instrumental delivery; (4) where breast feeding is not possible; (5) when any cerebral symptoms develop during the first few days of life; (6) in cases of hæmorrhagic diathesis, icterus gravis neonatorum, and anæmia; and (7) where an operation is necessary on the newborn.—A. I. S. Macpherson *et al.*, *Brit. med. J.*, i/1940, 839.

It is probable that for all practical purposes, methyl-naphthoquinone will replace both vitamin K<sub>1</sub> and vitamin K<sub>2</sub>. Its stability is about the same as that of vitamin K<sub>1</sub> though it is less photolabile. In clinical use there are three possible routes. First, orally; second, intravenous, in diluted aqueous alkalisied solution, where this can be prepared; third, intramuscular or subcutaneous, in an oil solution.—A. L. Bacharach, *Analyst*, 1940, 13.

**Synthetic phthiocol** has been administered to 10 patients exhibiting hypoprothrombinæmia and in each instance the elevated prothrombin clotting time has been reduced to a near normal level.—H. R. Butt *et al.*, *Proc. Mayo Clin.*, 1939, 497.

**Prokayvit Oral** (*British Drug Houses, London*). Tablets and capsules containing 10 mg. of diacetyl-2-methyl-1:4-naphthohydroquinone, a substance with therapeutic properties similar to those of vitamin K. The capsules, containing an oily solution of the substance, are intended for administration to infants, the point being cut off and the contents either added undiluted to the feed or mixed with about one teaspoonful of olive oil. *Dose*.—5 to 10 mg.

**Vitamin P.** Cases of hæmorrhagic purpura of the vascular type were successfully treated with vitapric, an impure concentrate of ascorbic acid obtained from paprika. Similar results were not obtained with ascorbic acid, and search for the active principle led to the isolation of a flavone glucoside called citrin or, since it appeared to exert a specific regulating influence on the permeability of vessels, vitamin P (vitamin of permeability). Citrin was found to consist of a mixture of hesperidin and an eriodictyol glucoside, but the name vitamin P has also been applied to the former. It is also found in hips and lemon juice, always in the presence of ascorbic acid, but although a number of papers have been published on its therapeutic uses, many investigators still deny the existence of a substance with the properties of vitamin P as distinct from ascorbic acid.

Oral administration of hesperidin, in doses of 1 gramme daily, can reduce the number of hæmorrhages in patients with vitamin deficiency.—H. Scarborough and C. P. Stewart, *Lancet*, ii/1938, 610.

Injections of vitamin P, in the form of daily intravenous injections of 50 mg. of citrin, brought about complete disappearance of all symptoms in a woman of 22 who had suffered from Schönlein-Henoch purpura for eight years, after treatment with ascorbic acid had failed to affect the disease. The purpura relapsed when the administration of citrin was stopped.—T. Jersild, *Lancet*, i/1938, 1445.

The evidence upon which the existence of vitamin P is based has been reviewed and it has been shown that a conclusion as to the reality of such a vitamin cannot be maintained on the basis of the published work. Evidence is adduced from experiments on human subjects which establishes the existence of a factor decreasing capillary fragility.—H. Scarborough, *Biochem. J.*, 1939, 33, 1400.

**Permidin** (*Glaxo Laboratories, London*). Tablets containing 0.25 g. of hesperidin (vitamin P). *Dose*.—1 to 4 tablets daily. Disorders involving increased permeability or fragility of the capillaries. Used in purpuric eruptions following bismuth and arsenical treatment of syphilis.

**ACIDUM BENZOICUM***B.P., U.S.P. XI, Fr. Cx., P. Helv. V, etc.* $C_6H_5 \cdot COOH = 122.12.$ *Dose.*—5 to 15 grains (0.3 to 1 g.).

*Manufactured* either from gum benzoin (natural) or from toluene (synthetic), the former being the more expensive. White feathery crystals; m.p. 121°; sublimes at 150°.

*Soluble* 1 in 450 of water, 1 in 3 of alcohol 90%, 1 in 7 of chloroform, 1 in 3 of ether, 1 in 30 of carbon disulphide, and 1 in 30 of glycerin; very soluble in fats and oils.

*Incompatible* with ferric salts and mercuric chloride.

*Uses.* Benzoic acid, taken internally, is so irritant to the gastric mucosa that it is seldom employed in this manner except as a constituent of expectorant mixtures. It has been employed as a urinary antiseptic, *e.g.*, in cystitis, but its antiseptic action on the urine is even weaker than that of the salicylates. It acidifies the urine, being mainly excreted as hippuric acid, but it is mostly employed for this purpose in the form of one of its salts. In concentrations of 1 in 1000 it inhibits the growth of most moulds and bacteria and may be used as a preservative in pharmaceutical preparations having an acid or neutral reaction. In the form of compound benzoic acid ointment it is of value in the treatment of ringworm.

Four grains of benzoic acid with 1 grain of Canada balsam, or 1 minim of glycerin, makes a good pill.

A 1 in 20 solution in alcohol relieves urticaria, and, as an antiseptic lotion or gargle, 1 dissolved in 500 of water is employed.

*Collutorium Acidi Benzoici (R.D.H.).*

*Dose.*—One tablespoonful in a tumblerful of water.

Benzoic acid 10 gr., tincture of krameria 15 m., saccharin 6 gr., oil of peppermint 2 m., oil of cinnamon 2 m., alcohol 90% to 1 oz.

*Miller's Mouth Wash* is similar.

**Trochisci Acidi Benzoici (B.P.C.).**

Contain  $\frac{1}{2}$  grain with fruit basis; are also obtainable with simple basis. Those of *T.H.* have a red currant basis. Useful as a voice lozenge.

**Unguentum Acidi Benzoici Compositum (B.P.C.).** *Syn.* WHITFIELD'S OINTMENT.

Contains benzoic acid 5% and salicylic acid 3% in white soft paraffin and coconut oil. A valuable treatment for ringworm of the scalp, body or nails.

**Ung. Acid. Benzoic. Co. (N.I.F.).** *Syn.* WHITFIELD'S OINTMENT (N.I.F.). Contains benzoic acid 24 gr., salicylic acid 15 gr., hard paraffin 66 gr., simple ointment 66 gr., coconut oil to 480 gr.

**Unguentum Acidi Benzoici et Acidi Salicylici Forte (K.C.H.).** also with *syn.* WHITFIELD'S OINTMENT, contains benzoic acid 1 dr., salicylic acid 30 gr., soft paraffin 2 dr., coconut oil to 1 oz.

**Ammonii Benzoas (B.P.C., U.S.P. XI, P. Helv. V).**

 $C_6H_5 \cdot COONH_4 = 139.14.$ 

*Dose.*—5 to 15 grains (0.3 to 1 g.).

In colourless laminar crystals: **soluble** 1 in 6 of cold water, 1 in 30 of alcohol, and 1 in 8 of glycerin.

Useful expectorant in chronic bronchitis; also used for increasing the acidity of the urine in cystitis, catarrh of the bladder and phosphaturia.

[P1] **Mistura Boro-Benzoatis** (K.C.H.).

Ammonium benzoate 20 gr., boric acid 10 gr., tincture of hyoscyamus 30 m. infusion of buchu to 1 oz. A useful urinary antiseptic mixture.

**Magnesii Benzoas.**  $(C_6H_5 \cdot COO)_2Mg = 266.54$ .

*Dose.*—5 to 15 grains (0.3 to 1 g.).

White crystalline powder. Soluble 1 in 30 of water, hardly soluble in alcohol 90%.

**Incompatible** with acids, also with sodium bicarbonate.

Antipyretic. Used as an anti-arthritis for rheumatism and as a cathartic in cirrhosis of the liver.

**Potassii Benzoas.**  $C_6H_5 \cdot COOK, 3H_2O = 214.25$ .

*Dose.*—5 to 30 grains (0.3 to 2 g.).

White crystals. Soluble 1 in  $1\frac{1}{2}$  of water and 1 in 20 of alcohol 90%. Uric acid solvent.

**Sodii Benzoas** (B.P., Fr. Cx., P. Ital. V, U.S.P. XI, P. Helv. V., P. Jap. V).

$C_6H_5 \cdot COONa = 144.11$ . P. Ned. V has  $\frac{1}{3}$  mol.  $H_2O$ .

*Dose.*—5 to 30 grains (0.3 to 2 g.). U.S.P. XI average dose 15 grains.

In white granular crystals or in powder. Soluble 1 in 2 of water and about 1 in 50 of alcohol 90%.

Two varieties are made, one from the acid obtained from benzoïn, the other from the synthetic acid.

**Incompatible** with mineral acids and with ferric salts. It is apt to cause gastric irritation if taken on an empty stomach.

**Uses.** Urinary antiseptic. Acute lacunar tonsillitis is stated to be cured by it in 12 to 36 hours if given in 5 to 15 grain doses every 2 hours. In pyelitis due to *B. coli* infection, sodium benzoate combined with hexamine has given good results.

**Phenylsemicarbazide** (Fr. Cx.). *Prop. Name.* CRYOGÉNINE (*Lumière, Lyons; Anglo-French Drug Co., London*).  $C_6H_5NH \cdot NH \cdot CONH_2 = 151.17$ .

F.E. VIII includes *m*-benzaminosemicarbazide to which the proprietary name "Crigénina" is attached.

*Dose.*—3 to 24 grains (0.2 to 1.5 g.), up to 40 grains (2.5 g.) per day.

In white crystals soluble 1 in 100 of water, 1 in 25 of alcohol 90%. Antipyretic and analgesic for rheumatism, neuralgia, etc.

**Benzoinum** (B.P.).

*Dose.*—10 to 30 grains (0.6 to 2 g.).

The balsamic resin from *Styrax Benzoin* (Sumatra benzoin), containing 19 to 29% of free balsamic acids and not more than 60% of total balsamic acids, calculated on the dry alcohol-soluble matter. U.S.P. XI and P. Jap. V allow also Siam benzoin, from *S. tonkinense* or other species. Fr. Cx., P. Dan. and P. Helv. V allow Siam benzoin only.

Benzoin acts as a stimulating expectorant, but it is seldom given internally as such.

**Vap. Benzoin Co. c. Menthol** (N.I.F.).

Menthol 8 gr., benzoin 48 gr., storax 34 gr., balsam of tolu 12 gr., industrial methylated spirit to 1 oz. For use add 1 dr. to a pint of boiling water and inhale the vapour.

**Tinctura Benzoini Simplex (B.P.C.).**

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

1 in 10 of alcohol 90%. *P. Ital. V* 1 in 5 of alcohol 80%.  
One of the tincture in rose water 40, is useful as a face lotion in urticaria and in irritable conditions of the skin.

**Tinctura Benzoini (U.S.P. XI).**

*Average dose.*—15 minims (1 ml.).

Benzoin (Sumatra or Siam) 1 in 5, in alcohol, 95%. *Fr. Cx.* is similar but made with alcohol 80%.

**Lotio Benzoini (B.P.C.). Syn. LAIT VIRGINAL.**

Tincture of benzoin, 1 in 40, in rose water.

**Nebula Benzoini Composita (B.P.C.).**

Menthol 1% with oils of eucalyptus, cassia and pumilio pine in glycerin and tincture of benzoin. Useful in nasal and bronchial catarrh.

**Tinctura Benzoini Composita (B.P.). Syn. FRIARS' BALSAM, TRAUMATIC BALSAM.**

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Benzoin 10%, with storax, aloe and balsam of tolu in alcohol 90%.

A drachm to a pint of hot water is valuable as an inhalation in bronchitis and acute laryngitis. Undiluted it is used as a wound dressing. Is useful internally in chronic bronchitis. Mixtures require the addition of 1 dr. per oz. of mucilage of acacia, or of a mixture of equal parts of mucilages of acacia and tragacanth, to suspend the resins.

**Tinctura Benzoini Composita (U.S.P. XI).**

*Average dose.*—30 minims (2 ml.).

Benzoin 10, aloe 2, storax 8, tolu 4, in alcohol 95%.

**Collunarium Benzoini (T. H.).**

Compound tincture of benzoin 5 m., borax 5 gr., water to 1 oz.

**Benzyl Alcohol.  $C_6H_5 \cdot CH_2OH = 108.13$ .**

*Dose.*—5 to 40 minims (0.3 to 2.5 ml.) in water 3 or 4 times a day.

A liquid with a slight aromatic odour. Has been employed as a local anæsthetic, by application or subcutaneous injection, in a 1 to 4% dilution in distilled water or normal saline solution, but is stated to be irritant locally. A few drops on an exposed nerve or cavity is an efficient anodyne for toothache.

**Benzylis Benzoas (B.P.C., P. Dan., F.E. VIII).**

*Syn. and Prop. Name.* SPASMODYN (*Bush, London*), ESTER BENCYLBENZOICO, PERUSCABINA.  $C_6H_5 \cdot COOC_6H_5 = 212.1$ .

*Dose.*—5 to 8 minims (0.3 to 0.5 ml.) as a 1 in 5 alcoholic solution in water, or in capsules, or as an emulsion.

White crystals with faint aromatic odour and burning taste, m.p. 20°, b.p. about 323°.

**Insoluble** in water and glycerin; miscible with alcohol, chloroform and ether.

**Uses.** It is practically non-toxic and has been used in excessive intestinal peristalsis, diarrhœas and dysentery, intestinal, biliary and renal colic, spastic constipation, vesical spasm, uterine colic, dysmenorrhœa, persistent hiccough, arterial spasm and bronchial spasm of true asthma. Sometimes of value in whooping-



cough but its action is uncertain. Externally it has proved of value in the treatment of scabies; Kissmeyer's original formula (*Lancet*, i/1937, 21) consisted of equal parts of benzyl benzoate, isopropyl alcohol and soft soap, but this has since been modified by the use of industrial methylated spirit in place of the isopropyl alcohol (*vide infra*).

**SCABIES.** The following treatment has been used in Denmark for a number of years and has replaced sulphur ointment. The patient takes a hot bath, after which a solution made up of benzyl benzoate 50 g., liniment of soft soap 65 g., alcohol (90%) 30 g., and distilled water 5 g., is applied over the entire body with a small brush and allowed to dry. Another layer is then applied in similar fashion. After the skin is dry the patient dresses. After another bath the next day he changes to fresh clothing. The treatment is preferable to the sulphur treatment in that it is odourless and non-irritating.—L. Goldman, *Arch. Derm. Syph.*, N. Y., 1937, 36, 140.

Anoint the body with soft soap, rubbing it carefully into those parts commonly attacked by the acarus. Then soak for ten minutes in a bath at 100°F., rubbing the affected areas thoroughly during this time. While the body is still wet apply the following lotion vigorously for 5 minutes by means of a pig-bristle shaving brush: Equal parts of benzyl benzoate, industrial spirit and soft soap (B.P.). Allow the lotion and the lather produced to dry on the skin and again apply the lotion vigorously for a further 5 minutes, then dry the body with a towel and resume the clothes worn before treatment. 24 hours later a bath is taken and clean clothes are put on and the discarded clothing and bedclothes used by the patient sterilised by boiling. Other members of the family should be treated on the same day even though they show no signs of the disease. It is a safe, reliable and rapid treatment causing a minimum of inconvenience and discomfort.—R. E. King, *Brit. med. J.*, ii/1940, 626.

**Proscabin** (Bayer Products, London). Benzyl benzoate emulsion for the local treatment of scabies.

**Benzoylis Peroxidum.**  $C_6H_5 \cdot CO \cdot O_2 \cdot CO \cdot C_6H_5 = 242.1$ . A crystalline compound, m.p. 103.5°, prepared by the interaction of 100 of sodium peroxide and 180 of benzoyl chloride, at a low temperature. Soluble slightly in water, more so in alcohol.

**Uses.** As a dusting powder, as a 2 to 3% solution in oil, or as an ointment in soft paraffin, for burns, ulcers and for dermatitis due to the poison ivy (*Rhus toxicodendron*).

**Benzylis Succinas (B.P.C.). Prop. Name.** SPASMINE (Bush, London).

$(CH_2 \cdot COOCH_2 \cdot C_6H_5)_2 = 298.1$ .

**Dose.**—5 to 15 grains (0.3 to 1 g.) in tablets or capsules.

This is a tasteless crystalline substance, **soluble** in alcohol, ether, chloroform, and fixed and volatile oils, almost insoluble in water. Not nauseating to the stomach. It is employed for conditions similar to those for which the benzoate has been given.

[P1-81] **Spasticine** (Napp, London). Tablets containing benzyl succinate 0.3 g., papaverine hydrochloride 0.03 g., atropine methylbromide 0.0005 g.

**Dose.**—From 1 to 3 tablets three times a day. Antispasmodic.

**Acidum Hippuricum.** *Syn.* BENZAMINO-ACETIC ACID, BENZOYL GLYCOCOLL.  $C_6H_5 \cdot CONH \cdot CH_2 \cdot COOH = 179.1$ .

**Dose.**—5 to 20 grains (0.3 to 1.2 g.).

This acid, occurring as white crystals, **soluble** in hot water (very slightly in cold—about 1 in 600), melting at 187°, may be prepared from the urine of herbivora, also synthetically by treating aminoacetic acid with benzoyl chloride or benzoic anhydride.

**Ammonii Hippuras (B.P.C.).**  $C_9H_8O_3N(NH_4) = 196.1$ .

*Dose.*—5 to 20 grains (0.3 to 1.2 g.).

Small white or brownish-white deliquescent crystals. Soluble in water, and 1 in 20 of alcohol 90%. This and other hippurates (sodium, potassium and lithium) have been given in gouty conditions. They are also administered, with other substances, in the treatment of arterial hypertension.

**Acidum Cinnamicum (B.P.C.).** *Syn.* PHENYLACRYLIC ACID, CINNAMYLIC ACID.  $C_6H_5 \cdot CH : CH \cdot COOH = 148.1$ .

*Dose.*—2 to 3 grains (0.12 to 0.2 g.) by mouth;  $\frac{1}{80}$  to  $\frac{1}{3}$  grain (0.0013 to 0.02 g.) by hypodermic injection, in oily solution.

Transparent micaceous crystals, m.p.  $132^\circ$  to  $135^\circ$ , slightly soluble in water, soluble in alcohol, ether and oils. Has been used to induce leucocytosis. Mostly given as the sodium salt.

**Æthylis Cinnamas.**  $C_6H_5 \cdot CH : CH \cdot COOC_2H_5 = 176.2$ . A solution of ethyl cinnamate in benzyl alcohol, corresponding to 5% of benzyl cinnamate, and olive oil, has been used in a dose of 0.25 ml. intramuscularly in the treatment of all forms of tuberculosis. It is contraindicated in nephritis.

**Sodii Cinnamas (Fr. Cx.).** *Syn.* HETOL.

$C_6H_5 \cdot CH : CH \cdot COONa = 170.1$ .

*Dose.*—2 to 5 grains (0.12 to 0.3 g.).

A white crystalline powder with faint aromatic odour. **Soluble** 1 in 11 of water, 1 in 10 of glycerin, 1 in 160 of alcohol 90%. Has been administered orally or hypodermically in the treatment of tuberculosis.

**Glycerinum Sodii Cinnamatis.**

*Dose.*—30 to 60 minims (2 to 4 ml.), by injection. A 10% solution in glycerin, made by heating to not exceeding  $180^\circ$ . Has been used hypodermically and intravenously in tuberculosis and cancer; it causes a general leucocytosis.

**Cinnaldehydum.** *Syn.* CINNAMAL.  $C_6H_5 \cdot CH : CH \cdot CHO = 132.1$ .

*Dose.*—1 minim.

The aldehyde occurring in cinnamon oil. A colourless liquid with cinnamon odour. Sp. gr. 1.054 to 1.056. Soluble in alcohol in all proportions.

**Capsules (Gelatin),** 1 minim, have been used in malignant disease and in tuberculosis, especially in pulmonary cases.

**Acidum Coumaricum.** *Syn.* o-HYDROXYCINNAMIC ACID.

$C_6H_4(OH) \cdot CH : CH \cdot COOH = 164.1$ .

Brownish crystals, m.p.  $200^\circ$ . The *meta*- acid melts at  $191^\circ$ , and the *para*- at  $206^\circ$ .

**Soluble** very slightly in water and chloroform, 1 in 12 or less of alcohol, 1 in 36 of ether. The coumarates have action of vasodilators, and they may be taken for prolonged periods without harm.

**Injectio Sodii o-Coumaratis.** A 22% aqueous solution of sodium o-coumarate,  $C_6H_7O_3Na$ . Has been used in cancer and tuberculosis.

*Dose.*—25 minims (1.5 ml.), thrice weekly when possible between the growth and healthy subjacent tissues or in the course of lymphatics proceeding from the region of the growth, or over a large serous sac like the peritoneum. In glandular and early cases of pulmonary tuberculosis Drage reported good results. In cancer he held that few drugs exert more definite action.

**Coumarin.** *Syn.* COUMARIC ANHYDRIDE.  $C_9H_6O_2 = 146.14$ .

The lactone of coumaric acid. In colourless crystals with aromatic odour and taste; contained in tonquin beans, also in woodruff. It is made synthetically by boiling salicylic aldehyde with acetic anhydride and sodium acetate. Soluble

in alcohol, ether and oils, but not to any extent in water. Sublimes unchanged. One part will disguise the odour of 50 of iodoform.

**Tonco Semen** (B.P.C.). *Syn.* TONKA or TONQUIN BEANS.

The seeds of *Dipteryx odorata* and of *D. oppositifolia* (Leguminosæ), dried in the sun or cured by immersion in rum for a few days and drying. Formerly used as a source of coumarin; also used in perfumery.

**Vanilla** (B.P.C., *Fr. Cx.*) consists of the cured capsular fruits of *V. planifolia* (Orchidacæ). Contains 2 to 3% of vanillin and other unknown aromatic substances.

**Tinctura Vanilla** (*Fr. Cx.*). Macerate vanilla (1 to 10) in alcohol 80% for 10 days.

**Vanillinum** (B.P.C., U.S.P. XI, *Fr. Cx.*, *P. Helv. V*).

*Syn.* VANILLIC ALDEHYDE, METHYLPROTOCATECHUIC ALDEHYDE, HYDROMETHOXYBENZALDEHYDE.  $\text{CH}_3\text{O} \cdot \text{C}_6\text{H}_4(\text{OH}) \cdot \text{CHO} = 152 \cdot 1$ .

White crystalline needles with intense vanilla odour and taste. Can be extracted from vanilla, but is usually prepared synthetically from eugenol.

**Soluble** in most organic solvents; slightly soluble in water, more soluble in hot water; readily soluble in alkalis.

Use suggested in atonic dyspepsia as an excito-motor stimulant. For employment in Gunzburg's test, *vide Vol. II. Solutio Vanillini*—Vanillin 80 gr., alcohol 90% to 1 oz. For ordinary purposes  $\frac{1}{2}$  dr. will flavour a pint of medicine. **Essence of Vanilla** 1 in 8 by macerating vanilla beans 1 finely ground with sand 1, in a mixture of water 2, and alcohol 90% 6.

**Elixir Vanillini Compositum** (N.F. VI). *Dose.*— $\frac{1}{2}$  to 1 drachm. Mix compound spirit of vanillin 20, with 95% alcohol 80, add glycerin 25, then syrup 300, caramel 2, and water to 1000. Filter.

**Spiritus Vanillini Compositus** (N.F. VI). *Dose.*— $\frac{1}{2}$  to 1 drachm. Vanillin 40, oil of orange 10, oil of cardamom 2, oil of cinnamon 1, are dissolved in a sufficiency of alcohol 95% to make 200.

**Agaricus** (B.P.C.). *Syn.* POLYPORUS OFFICINALIS, BOLETUS LARICIS, FUNGUS LARICIS (*P. Austr.*, *P. Ital. V*), AGARIC BLANC (*Fr. Cx.*), POLYPORE DE MÉLÈZE (*Fr. Cx.*), PURGING AGARIC.

*Dose.*—3 to 30 grains (0.2 to 2 g.).

The dried fungus *Fomes officinalis*, in light, spongy pieces. Large doses purgative, small ones astringent. For night sweats, diarrhoea and to diminish bronchial secretion. *Tincture, dose.*—20 to 60 minims, 1 in 10 of 60% alcohol. *Extract, dose.*— $\frac{1}{2}$  to 2 grains, prepared by exhaustion with 60% alcohol, about 6%.

**Agaricus** (B.H.P.). *Syn.* AGARICUS MUSCARIUS, FLY AGARIC. The entire fresh fungus, *Amanita muscaria*. It has a slight, unpleasant odour, a bitter taste and is very poisonous. It contains the poisonous base muscarine, a toxin and a colouring matter muscarufin. Used in homœopathic medicine in the treatment of chorea, skin irritation, neuralgia and chilblains.

**Acidum Agaricum** (B.P.C., P.G. VI, *P. Ital. V*, *P. Helv. V*, *P. Jap.*, *P. Dan.*). *Syn.* AGARICIN, LARICIC ACID.

$\text{CH}_2\text{C}(\text{OH})\text{CH}(\text{C}_{16}\text{H}_{33})(\text{COOH})_3, 1\frac{1}{2}\text{H}_2\text{O} = 443 \cdot 3$ .

*Dose.*— $\frac{1}{2}$  to  $\frac{1}{4}$  grain (0.005 to 0.03 g.). P.G. VI, *P. Helv. V* and *P. Ital. V* have max. single dose  $1\frac{1}{2}$  gr.

Obtained from the fungus, *Fomes officinalis*, growing on larch trees. An odourless, tasteless microcrystalline powder, **soluble** 1 in 130 of water. Given to restrain the night sweats of phthisis. Owing to slow absorption should be given some hours before retiring.

**Amadou.** *Syn.* OAK AGARIC, SURGEON'S AGARIC, TOUCHWOOD. *Polyporus fomentarius* L. A fungus prepared with alkali and nitre, in light brown elastic pieces. Employed as a mechanical hæmostatic. It is included in *P. Austr.* under the name *Fungus ignarius*.

## ACIDUM BORICUM

*B.P., U.S.P. XI, P. Helv. V, Fr. Cx., etc.*  
 $\text{H}_3\text{BO}_3 = 61.84.$

*Syn.* BORACIC ACID, HYDROGEN BORATE, SAL SEDATIVA DE HOMBERG (*F.E. VIII*).

*Dose.*—5 to 15 grains (0.3 to 1 g.).

In white laminar crystals, with bitter taste, or as powder (that known as *Pulv. Acid. Boric. Subtilis* has been passed through a No. 170 sieve). The crystals yield a clearer solution than the powder.

**Soluble** 1 in about 25 of water, 1 in 3 of boiling water, 1 in 30 of 90% alcohol, 1 in 5 of glycerin at 0°, 7 in 10 at 100°, slightly soluble in volatile oils. Insoluble in ether.

**Antidotes.** Empty stomach by stomach tube or emetic. Give purgative dose of magnesium sulphate. A teaspoonful taken in error has caused death. Used for lavage, it may prove poisonous owing to idiosyncrasy, producing a rash.

Fifty per cent. of the acid administered is excreted in the urine within 12 hours, the rest remains in the body for 3 to 4 days and hence may accumulate under repeated dosage.

Fatal poisoning of babies each weighing about 7 lbs. with from 0.8 to 3 g. of boric acid given in solution in error for water.—*Pharm. J.*, i/1927, 361.

Recovery of a woman of 42 from an intravenous injection of 600 ml. of a 2.5% solution of boric acid (*i.e.*, approx. 15 g.) in 10% dextrose, given post-operatively after hysterectomy in mistake for 10% dextrose. Immediately following discovery of the error 1000 ml. of 10% dextrose was given intravenously. The patient only vomited once, the pulse remained regular and strong and the respirations were unchanged. At the end of 10 days the patient was discharged. It is concluded that when renal excretion is normal boric acid injected intravenously in large amounts does not produce appreciable symptoms of toxicity.—A. R. McIntyre and C. J. Burke, *J. Pharmacol.*, 1937, 60, 113.

**Incompatible** with tannin.

**Uses.** Antiputrefactive and mildly antiseptic. Has been given as antiseptic before and after bladder operations, in typhoid, and also for cystitis. It is used as a dressing to wounds, sores, and the skin generally. When mixed with starch, with or without zinc oxide, it forms a useful "dusting powder" for infants, etc. A little in the socks prevents the odour of perspiring feet.

Vomiting in gastric dilatation or gastric catarrh of infants has been treated by washing out the stomach with weak boric acid

lotion. In otorrhœa an alcoholic solution of boric acid may be used.

Though not actually germicidal it is an excellent cleanser, especially for lavage of cavities in which sterile water or saline solution would be more irritating. The absence of all toxic effect makes it an ideal irrigating fluid where bulk is desirable for cleansing or distension. Though not a disinfectant, even in saturated solution, it checks putrefaction and decomposition in a solution of 0.3%. In urologic practice it is used as a routine by many for cleansing the bladder and urethra before an instillation of some antiseptic substance.—H. W. E. Walker, *J. Amer. med. Ass.*, ii/1938, 1465.

**A.B.C. Powder.** Boric acid, bismuth subnitrate and calomel, equal parts. A stimulant antiseptic dusting powder.

**Carbasus Acidi Borici (B.P.C.).** *Syn.* BORIC GAUZE.

Contains 10 to 20% of boric acid.

**Cataplasma Acidi Borici (B.P.C.).** 20% in linseed poultice.

**Cataplasma Acidi Borici et Carbonis (B.P.C.).** 4% of each in slippery elm poultice.

**Cataplasma Amyli et Acidi Borici (B.P.C.).** Boric acid 6% in starch poultice.

**Collyrium Acidi Borici (B.P.C.).** 2% w/v.

**Collyr. Acid. Boric. (N.I.F.).** Boric acid 12.5 gr., distilled water to 1 oz.

**Collyrium Acidi Borici et Zinci (B.P.C.).** Contains 4 gr. of boric acid and 1 gr. of zinc sulphate per oz.

**Collyr. Zinci Co. (N.I.F.).** Boric acid 5 gr., zinc sulphate 1 gr., distilled water to 1 oz.

**Glycerinum Acidi Borici (B.P.).**

*Syn.* GLYCERITE OF BOROGLYCERIN (*U.S.P. XI*).

*Dose.*—10 to 30 minims (0.6 to 2 ml.).

Consists of glyceryl borate and glycerin, and contains the equivalent of 31% w/w of boric acid.

It is readily miscible with water and alcohol. Of value in otorrhœa.

**Boroglycerinum (B.P.C.)** is a similar preparation containing the equivalent of 50% w/w of boric acid.

**Gossypium Acidi Borici (B.P.C.).** *Syn.* BORIC WOOL.

Contains 15 to 30% of boric acid. *P. Jap. V* has about 10%.

**Aurist. Boric. (N.I.F.).** Glycerin of boric acid 120 m., industrial methylated spirit 100 m., glycerin to 1 oz.

**Guttæ Spiritus (T.H.).** Rectified spirit 1 dr., boric acid 10 gr., water to  $\frac{1}{2}$  oz. The strength of the spirit may be gradually increased until pure spirit is used.

**Lintum Acidi Borici (B.P.C.).** *Syn.* BORIC (BORACIC) LINT. Contains 35 to 45% of boric acid.

The following simple procedure is equally successful for the treatment of all wounds from a pinprick to a compound fracture. The technique consists in the application of wet boric lint to the surface of the wound. The boric lint must contain equal parts by weight of boric acid and lint. Immediately before being applied it must be saturated with cold water and not wrung out. The entire area of the wound is covered with this wet lint, on top of which is placed oiled silk, which must entirely cover the lint to seal it off hermetically and keep it from becoming dry. The dressing is kept in place with a bandage or towel.—P. Weatherbe, *Lancet*, ii/1939, 1317.

**EPIDERMOPHYTOSIS.** Trichophyton infection (interdigital) cured by insertion of small strips of boric lint, about 1 inch by  $\frac{1}{2}$  inch, well pressed into the affected spaces and renewed night and morning.—*Brit. med. J.*, ii/1934, 889.

**Curatio Normalis II** (*B.P.C. Supp.*). *Syn.* STANDARD DRESSING No. 2, FOMENTATION DRESSING.

Boric acid lint 12 inches by 12 inches, absorbent cotton-wool 240 gr., oiled cambric 6 inches by 6 inches, open-weave bandage 2 inches by 4 yards.

**Curatio Normalis III** (*B.P.C. Supp.*). *Syn.* STANDARD DRESSING No. 3, SMALL ELASTIC ADHESIVE WOUND DRESSING.

The dressing consists of a pad, composed of one-ply muslin bandage wrapped round a strip of absorbent lint, fixed to a base of elastic adhesive cotton fabric. The pad measures  $\frac{3}{4}$  inch by 1 inch, and is medicated with about 5% of boric acid and tinted pink. The elastic cotton fabric is flesh-coloured and measures  $1\frac{1}{2}$  inches by 2 inches, and is spread with a rubber adhesive compound containing not less than 20% of zinc oxide.

**Curatio Normalis IV** (*B.P.C. Supp.*). *Syn.* STANDARD DRESSING No. 4, MEDIUM ELASTIC ADHESIVE WOUND DRESSING.

Similar to Standard Dressing No. 3, but the pad measures  $1\frac{1}{2}$  inches by 2 inches, and the elastic cotton fabric 2 inches by 3 inches.

**Curatio Normalis V** (*B.P.C. Supp.*). *Syn.* STANDARD DRESSING No. 5, LARGE ELASTIC ADHESIVE WOUND DRESSING.

Similar to Standard Dressing No. 3, but the pad measures  $1\frac{1}{2}$  inches by 2 inches, and the elastic cotton fabric  $2\frac{1}{2}$  inches by  $3\frac{1}{2}$  inches.

**Curatio Normalis VI** (*B.P.C. Supp.*). *Syn.* STANDARD DRESSING No. 6, EXTRA LARGE ELASTIC ADHESIVE WOUND DRESSING.

Similar to Standard Dressing No. 3, but the pad measures  $2\frac{1}{2}$  inches by  $3\frac{1}{2}$  inches, and the elastic cotton fabric  $3\frac{1}{2}$  inches by  $4\frac{1}{2}$  inches.

**Curatio Normalis VII** (*B.P.C. Supp.*). *Syn.* STANDARD DRESSING No. 7, FINGER DRESSING.

The dressing consists of an open finger-stall, made from two pieces of boric acid lint each 2 inches by  $1\frac{3}{4}$  inches, sewn to an open-weave bandage measuring 1 inch by 24 inches.

**Curatio Normalis VIII** (*B.P.C. Supp.*). *Syn.* STANDARD DRESSING No. 8, MEDIUM MEDICATED WOUND DRESSING.

The dressing consists of a pad sewn to an open-weave bandage measuring  $1\frac{1}{2}$  inches by 2 yards. The pad, which measures 3 inches by 4 inches, is composed of a piece of boric acid lint 3 inches by 4 inches, superimposed on about 25 gr. of absorbent cottonwool.

**Curatio Normalis IX** (*B.P.C. Supp.*). *Syn.* STANDARD DRESSING No. 9, LARGE MEDICATED WOUND DRESSING.

Similar to Standard Dressing No. 8, but the pad measures 4 inches by 6 inches, and is composed of boric acid lint 4 inches by 6 inches, superimposed on about 50 gr. of absorbent cottonwool. The open-weave bandage measures 3 inches by  $2\frac{1}{2}$  yards.

**Lotio Acidi Borici** (*B.P.C.*). 1 in 30. *N.I.F.* is similar.

A useful soothing antiseptic lotion for the eyes, bladder, vagina and mouth.

**Lotio Acidi Borici** (*R.L.O.H.*). 8 gr. to 1 oz. (2% approx.).

**Isotonic Boric Acid Lotion** is 3.1% strength—isotonic with the tears.

**Lotio Acidi Borici cum Zinci Sulphatis** (*R.L.O.H.*).

Boric acid 8 gr., zinc sulphate  $\frac{1}{2}$ , 1 or 2 gr., water to 1 oz.

**Oculentum Acidi Borici** (*B.P.C.*). 4% in simple eye ointment.

**Oculentum Acid. Boric.** (*N.I.F.*). Boric acid  $2\frac{1}{2}$  gr., white soft paraffin to 1 dr.

**Pessus Acidi Borici** (*B.P.C.*) contain 10 gr. (0.6 g.).

Convenient for replacing douches after delivery.

**Pessus Glycerini Acidi Borici** for vaginal use weigh 90 gr. each, and contain 70 gr. of glycerin of boric acid with gelatin 10 gr. and water 10 m.

**Pulvis Talci Boricus** (*B.P.C.*). Boric acid and starch, of each 10%, with purified talc, perfumed with oil of geranium.

**Solvellæ Acidi Borici** (*B.P.C.*) contain 15 gr. (1 g.).

**Suppositorium Acidi Borici** contains 3 gr. (0.2 g.) in each.

**Unguentum Acidi Borici** (*B.P.*). Boric acid 1, white paraffin ointment 9.

For cleansing the mouth and tongue in typhoid fever, the following ointment (Wyllie's ointment) is best:—Boric acid 60 gr., oil of peppermint 5 m., white soft paraffin to 1 oz. The ointment is applied by means of a soft badger tooth-brush. The mouth should be sprayed with hydrogen peroxide (10 vol.) before the ointment is used, and treatment should be carried out at least twice daily from the commencement of the disease.—S. Watson Smith, *Lancet*, ii/1936, 1453.

**Unguentum Acidi Borici** (*U.S.P. XI*).

Boric acid 10, wool fat 5, white wax 5, white petrolatum 80.

**Unguentum Acidi Borici Flavum** (*B.P.C.*). 10% in yellow soft paraffin.

**Unguentum Lano-Boricum Camphoratum.**

Boric acid ointment  $\frac{1}{2}$  oz., hydrous wool fat  $\frac{1}{2}$  oz., essential oil of camphor 20 m. For earache in children. Applied with a brush to the meatus.

**Borax** (*B.P., P. Helv. V, P. Dan., P. Jap. V*). *Syn.* SODII BORAS (*U.S.P. XI*), SODIUM BORATE (*Fr. Cx.*), BIBORATE, PYROBORATE or TETRABORATE.  $\text{Na}_2\text{B}_4\text{O}_7 \cdot 10\text{H}_2\text{O} = 381.4$ .

*Dose.*—5 to 15 grains (0.3 to 1 g.).

*Soluble* 1 in 25 of water, 1 in 1 of glycerin; insoluble in alcohol 90%.

**Incompatible** with cocaine hydrochloride, mercuric chloride, zinc sulphate, and other metallic salts. In these cases all incompatibility may usually be overcome by the addition of glycerin or by replacing half the borax with boric acid. Also incompatible with gums and mineral acids.

**Uses.** As gargle in diphtheria, for aphthæ, cancrum oris, and gangrenous stomatitis. As lotion in pruritus ani and vulvæ, in bromidrosis and fetid sweating of the feet. Gouty affections are treated with compresses of saturated solution.

Internally is frequently included in bromide mixtures as a sedative and for epilepsy.

**EPILEPSY.** Treatment consists essentially of borax 10 gr. and sodium bromide 10 to 15 gr. thrice daily. If the fits do not cease in a fortnight, the borax is increased to 15 gr. After 6 weeks 15 minims of belladonna tincture daily are given in addition if necessary, and after 2 months it is reduced and then omitted. The salt mixture is given for a year at least, when the bromide is gradually reduced. The patient then remains on borax for another year. This almost invariably achieves a cessation of fits in adults, but children do not, as a rule, respond so well.

**BILIARY COLIC.** Good results obtained in the treatment of pains due to pathological conditions of the biliary tract by intravenous injections of 10 ml. of a 5% aqueous solution of sodium baborate. Of 47 patients suffering from chronic cholecystitis pain disappeared completely in 28 and there was marked

improvement in it; there was also improvement in the general appearance, increase of appetite and gain in weight. A course of 20 daily injections was usually given and, if necessary, repeated after an interval. Strict diet adhered to during treatment and all other drugs eliminated. Care should be taken to avoid extravasation of the solution into the paravenous tissues, since this is followed by intense pain.—G. Macchioro, *per Practitioner*, ii/1939, 347.

**Collyrium Boracis (B.P.C.).** 1% w/v.

**Gargarisma Boracis (B.P.C.).** Borax 15 gr. per fl. oz.

**Glycerinum Boracis (B.P.).**

Borax 12% w/w in glycerin. Has an acid reaction and liberates carbon dioxide from carbonates. Is useful in infantile diarrhoea in 20 m. doses.

*Fatal poisoning* in two-weeks-old child following ingestion of 1½ drachms of borax and boric acid in the form of honey and borax and glycerin of borax: a dummy teat dipped in the latter may convey 1½ to 2 grains of borax to the child's mouth.—J. Birch, *Brit. med. J.*, i/1928, 177; *Lancet*, i/1928, 287.

**Liquor Alkalinus (B.P.C.).** *Syn.* COLLUNARIUM ALKALINUM. Borax and sodium bicarbonate 1 in 80 of each, with phenol and sucrose, in water.

**Liquor Boracis Compositus (B.P.C.).** *Syn.* DOBELL'S SOLUTION, COLLUNARIUM ACIDI CARBOLICI COMPOSITUM.

Borax and sodium bicarbonate 1 in 80 of each, with phenol, glycerin and water.

**Mel Boracis (B.P.).** *Syn.* BORAX HONEY, BORAX AND HONEY. Borax 10% in glycerin 5% and purified honey, all by weight.

**Pulvis Boracis Compositus (B.P.C.).** *Syn.* PULVIS ALKALINUS COMPOSITUS.

Equal parts of borax, sodium bicarbonate and sodium chloride.

**Pulvis Sodii Chloridi Compositus (B.P.C.).**

Equal parts of borax, sodium bicarbonate, sodium chloride and sucrose.

**Solvellæ Antisepticæ (B.P.C.).** *Syn.* EFFERVESCING MOUTH-WASH TABLETS.

Contain 3 gr. of borax with sodium benzoate, menthol, and other aromatics in an effervescing basis.

**Solvellæ Boracis Compositæ (B.P.C.).**

Contain borax 5 gr., sodium chloride and sodium bicarbonate of each 2½ gr., thymol  $\frac{1}{10}$  gr.

[P1] **Solvellæ Boracis et Benzaminæ Compositæ (B.P.C.).** *Syn.* TAB. NASO-PHARYNGEAL. CO. (N.I.F.), NASO-PHARYNGEAL SOLUTION-TABLETS.

Contain borax 3 gr., benzamine hydrochloride ½ gr., with sodium chloride, sodium benzoate, menthol, thymol and oil of sweet birch.

[D-P1-81] **Solvellæ Boracis et Cocainæ Compositæ (B.P.C.).**

Contain sodium chloride 5 gr., borax 3 gr., and cocaine hydrochloride  $\frac{1}{10}$  gr., with sodium benzoate, boric acid, menthol, thymol and oil of sweet birch.



**Sodii Boro-Tartras.** *Syn.* TARTARUS BORAXATUS.

*Dose.*—20 to 40 grains (1.2 to 2.5 g.).

Borax 2, potassium acid tartrate 5, water 15, evaporate until a little of the residue cooled is brittle. Powder and dry at 50°. Antiseptic and diuretic.

**Potassii Biboras.** *Syn.* POTASSIUM PYROBORATE.  $K_2B_4O_7 \cdot 5H_2O = 323.6$ .

Prismatic crystals, readily soluble in water.

Varicose and traumatic ulcers have been treated with tri-weekly application consisting of boric acid 63 g., potassium hydroxide 28 g., water 200 ml., starting with half-strength solution.

**Sodii Perboras** (B.P.C., *Fr. Cx.*, *F.E. VIII*, *U.S.P. XI*).  
 $NaBO_3 \cdot 4H_2O = 153.9$ .

*Dose.*—*U.S.P. XI* gives average dose 1 grain (0.06 g.).

A white permanent powder. **Soluble** in water, about 1 in 40, with decomposition, giving an alkaline solution containing free hydrogen peroxide. Is more soluble in solutions of boric, tartaric or citric acids, and in glycerin.

**Uses.** Antiseptic and deodorising. The dry salt may be used as a disinfectant, deodorant dusting powder. It has been used for soil-contaminated wounds. Tonsillitis occurring as complication in typhoid has been treated with sodium perborate gargle, 2 dr. to the pint.

To produce oxygenated water, 1 kilo yields 104 g., or about 72 litres of active oxygen. This quantity will produce 7 to 7.5 litres of "10 volume" oxygenated water. The solution is not acid. It contains hydrogen peroxide and borax. In practice, 170 g. with 60 g. of citric acid makes a litre of about "10 volume" strength. These solutions may be used to prepare antiseptic lotions, vaginal injections (about "5 volume" strength), *e.g.*, in leucorrhœa and metritis, and are useful in minor surgery.

Causes irritation and chemical burns variously ascribed to impurities, to sodium hydroxide formed by hydrolysis, and to flavouring agents. No harmful effects on the oral tissues were caused by a mixture of sodium perborate monohydrate, 30 parts, dehydrated monocalcium phosphate, 45 parts, tricalcium phosphate, 25 parts.—L. L. Manchey and S. Lee, *J. Amer. pharm. Ass.*, 1937, 890.

**PARONYCHIA.** Make a paste with sodium perborate and water. Gently work this in under the nail-fold with a cotton-tipped toothpick and also pack round the sides and under the nail. Draw on a rubber finger-cot and allow to remain overnight. The infected finger is then soaked three times a day in a warm solution of sodium perborate made by adding two teaspoonfuls to half a glass of water, and continue soaking as long as effervescence takes place. Cases usually cured in 3 to 8 weeks.—E. M. Rockwood, *New Engl. J. Med.*, i/1933, 295.

**VINCENT'S ANGINA.** Rapid cure in 95% of cases with 2% sodium perborate solution as a mouth wash. Best used as a thick paste and retained in the mouth for 4 or 5 minutes while oxidising froth develops.—*J. Amer. med. Ass.*, ii/1928, 247.

**Unguentum Sodii Perboratis.** 1% in paraffin ointment basis. Antiseptic and healing.

**Sodium Perborate Tooth Powder.** Sodium perborate 2%, in precipitated calcium carbonate.

There is no carefully controlled evidence that sodium perborate is beneficial to the gums, that it bleaches the teeth or that its use prevents diseases of the gums. Unless the powder and the alkali resulting from its decomposition be thoroughly removed, inflammation and necrosis of the oral membrane may result.—Rep. of Council on Dental Therapeutics of the American Dental Association, per *Pharm. J.*, ii/1935, 600.

**Calcii Perboras.** A bulky powder less stable than sodium perborate. Has been used in tooth powders.

**Magnesi Perboras** is similar.

**Magnesii Borocitras (B.P.C.).**

*Dose.*—15 to 30 grains (1 to 2 g.).

Dissolve light magnesium carbonate 70, in a solution of citric acid 100, in water 400, add boric acid 30, evaporate to dryness on a water bath and powder or scale. *B.P.C.* gives method of preparation from magnesium oxide.

A white powder or colourless scales, readily soluble in water; used as a urinary antiseptic internally for stone, gout, and rheumatism.

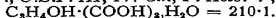
**Pulvis Magnesii Borocitratis Compositus (B.P.C.). *Syn.* BORACITE.**

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 g.).

Magnesium borocitrate 1, sucrose 2.

**ACIDUM CITRICUM**

*B.P., U.S.P. XI, Fr. Cx., P. Helv. V, etc.*



*Dose.*—5 to 30 grains (0.3 to 2 g.).

Colourless crystals or white powder, obtained from lemon juice, which contains as much as 7 to 9% (30 to 40 gr. per oz.), or prepared from glucose.

*Soluble* 2 in 1 of water, 1 in 2 of glycerin, 1 in  $1\frac{1}{2}$  of alcohol (90%), 1 in 8 of ether of sp. gr. 0.735, but much less soluble in 0.720 ether.

*Incompatible* with potassium tartrate and alkali carbonates.

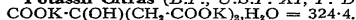
*Uses.* In dilute solution relieves thirst in fever. For other purposes is usually administered as alkali citrate.

**Collutorium Acidi Citrici (R.D.H.).**

Citric acid 10 gr., solution of formaldehyde 1 m., water to 1 oz. To be used on the tooth brush with an equal quantity of water.

**[P2] Lotio Acidi Citrici et Phenolis.**

Citric acid 3 dr., phenol  $\frac{1}{2}$  oz., water to 20 oz. For cleansing sockets after removing septic teeth.

**Potassii Citras (B.P., U.S.P. XI, P. Dan.).**

*Dose.*—15 to 60 grains (1 to 4 g.). *U.S.P. XI* average dose 15 grains.

White granular crystals obtained from citric acid and potassium carbonate.

*Uses.* It has diaphoretic, diuretic, and febrifuge properties. Is excreted as carbonate, rendering the urine alkaline, and is therefore given in cystitis, gout, and enuresis where the urine is over-acid. Large doses are useful for the acidæmia of diabetes. Is expectorant in the early stages of bronchitis and tracheitis with viscid, scanty secretion.

**Potassii Citras Effervescens (B.P.C.). About 1 in 6.**

*Dose.*—1 to 2 drachms (4 to 8 g.).

**Potassii Citras Effervescens (U.S.P. XI).**

*Average dose.*—1 drachm. Contains about 20% of potassium citrate.

**Sodii Citras** (B.P., U.S.P. XI, P. *Helv.* V, P. *Dan.*).  
 $\text{COONa} \cdot \text{C}(\text{OH})(\text{CH}_2 \cdot \text{COONa})_2 \cdot 2\text{H}_2\text{O} = 294 \cdot 1$ .

*Dose.*—15 to 60 grains (1 to 4 g.).

*Intravenously*, rabbits tolerate up to 0.4 to 1.6 g. per kilo, suitably diluted, or approximately 6.4 to 25.6 g. per 10-stone man (on Meeh's Formula, *q.v.*).

Granular crystals or powder. It is also obtainable with  $5\frac{1}{2}$   $\text{H}_2\text{O}$  (*Fr. Cx.*); 6 of the latter = 5 of the official salt.

Solution of sodium citrate 3.8% may be sterilised by the addition of Nipagin M 0.07 to 0.10% and Nipazol M 0.03% without recourse to heat.—T. Sabalitschka, *Pharm. Zentralh.*, 1938, 79, 151.

**Soluble.** 1 in less than 2 of water; insoluble in alcohol 90%.

**Uses.** Used for the same purposes as the potassium salt. It has anticoagulant properties and is added for this reason to blood in transfusion. Solutions of strength 3.8% are used for washing out syringes and apparatus in blood transfusion and for mixing with the blood at the time it is drawn from the vein. 40 ml. prevents coagulation of about 650 ml. of blood. Although an anticoagulant *in vitro*, it accelerates coagulation when injected intravenously as a 5 to 30% *w/v* solution, or intramuscularly in doses of 15 ml. of a 30% solution into each buttock. Intravenous injections should be made very slowly, using the finest possible needle.

Is used in feeding infants with cows' milk to prevent the formation of large clots, 1 gr. per oz. being added. Up to 3 gr. per oz. is sometimes used.

**Tabellæ Sodii Citratis** (B.P.C.) contain 2 gr. (0.12 g.).

**Liquor Sodii Citratis Fortis** (C.X.H.).

Sodium citrate 1 g., sterile water to 4 ml., which is sufficient to prevent the coagulation of 15 oz. of human blood.

**Wright's Solution.**

Sodium chloride 4, sodium citrate 1, water 120. For sinus washing.

**Bi-Citrol** (*Wilcox, Joseau, London*). Sodium dihydrogen citrate in granular powder. *Dose.*—1 teaspoonful in half a glass of warm water, twice daily. Hepatic and biliary affections, hyperviscosity of the blood, and arthritic affections.

[P1] **Citronin** (*Parke, Davis, London*).

*Dose.*—1 or 2 drachms at intervals of not less than 3 or 4 hours. A preparation containing in each drachm sodium citrate  $2\frac{1}{2}$  gr., citric acid  $\frac{1}{2}$  gr., potassium guaiacolsulphonate 1 gr., Cascara Evacuant  $\frac{1}{2}$  m., fluid extract of ipecacuanha  $\frac{1}{2}$  m., ethylmorphine hydrochloride  $\frac{3}{32}$  gr. For treatment of bronchitis and cough following "colds."

## ACIDUM FORMICUM

B.P.C., P. *Helv.* V.

$\text{H} \cdot \text{COOH} = 46 \cdot 02$ .

*Syn.* AMINIC ACID.

*Dose.*—2 to 10 minims (0.12 to 0.6 ml.) *per os* freely diluted, e.g., with mineral water. Hypodermically 2 to 15 minims of 1 in 1000 dilution of actual acid. It is better given as sodium salt.

A colourless liquid containing 24 to 26% *w/w* of  $\text{H}\cdot\text{COOH}$ , sp. gr. about 1.063. Miscible with water.

*Note.*—Formic acid is obtainable also of sp. gr.  $1.12=50\%$ ,  $1.15=65\%$ ,  $1.2=85\%$ ,  $1.22=100\%$   $\text{H}\cdot\text{COOH}$ ; as a rule the 25% acid is referred to. The stronger acids cause painful burns.

*Uses.* It is alleged that this acid (acting in a manner similar to cantharides) gives tone to the muscles and restrains muscular tremor, as in cases of paralysis agitans, and in chorea, and that it increases muscular energy and abolishes the sense of fatigue, but there is little scientific evidence in support of this. It is employed, usually as one of the salts, in influenza, gout, rheumatism, tremors, etc.

Intramuscularly a very dilute solution is valuable in rheumatic affections. The injections are much less painful than if given subcutaneously and the pain is transient.

The acid was originally made from the red ant, *Formica rufa*. The stinging nettle, *Urtica dioica*, contains formic acid, and has long been employed as a tonic and diuretic.

Given intramuscularly, gave definite improvement after 6 or 7 injections in rheumatic affections. Sixty cases treated.—*Brit. med. J. Epit.*, i/1933, 100.

*Estoform* (Crookes Laboratories, London). Orthoformic ester with extracts of wild cherry and senega in a glycerin-spirit base. *Dose.*—From 2 to 4 teaspoonfuls 3 times daily diluted with water. An antispasmodic in bronchitis, coughs and asthma.

**BEE VENOM.** Based on the suggestion that bee-keepers do not suffer from rheumatism, bee venom is employed therapeutically in the treatment of various rheumatic affections. The therapeutic action probably consists essentially in a stimulation of the metabolic processes in the tissues, favouring the breakdown of toxic products or their elimination. Injections in increasing dosage are administered intracutaneously at intervals of a few days over a period of some weeks, a preliminary test injection being made to test for idiosyncrasy. There is a temporary local irritation and swelling at the site of injection, accompanied by pyrexia, diuresis and drowsiness. The percutaneous administration of bee venom in ointment form is said to reduce the incidence of unpleasant reactions.

Very satisfactory results with bee venom. The venom collected at the end of the summer is most potent.—Frank Coke, *Brit. med. J.*, i/1934, 872.

Used at the Royal Devonshire Hospital with excellent results in arthritis, fibrositis and neuritis.—W. Shipton and J. B. Burt, *Brit. med. J.*, i/1934, 778.

Preparations are available (*Allen & Hanburys, London*, and *Antibody Products, Watford*) in ampoules for intramuscular injection and in ointment form for local use.

*Forapin* (Coates & Cooper, London). Bee venom available as an ointment and in ampoules of various strengths.

**Sodii Formas** (*B.P.C.*).  $\text{H}\cdot\text{COONa}$ ,  $\text{H}_2\text{O}=86.02$ .

*Dose.*—5 to 20 grains (0.3 to 1.2 g.) in solution, increased if desired to as much as 60 grains (4 g.) *per diem*.

A white alkaline powder soluble in water. A strong reducing agent and powerful antiseptic.

*Incompatible* with acids.

**Uses.** It is stated to have diuretic powers and to be non-toxic even in doses of 5 or 10 g. The formates were at one time thought to stimulate mental and physical activity, but there is no scientific evidence in support of this. Ocular fatigue has been treated with sodium formate instillation 1 in 50 to 1 in 30. Rheumatism has been improved by 15-grain doses.

[P1] **Elixir Formatum Compositum (B.P.C.).** *Syn.* ELIXIR FORMATUM CUM STRYCHNINA.

*Dose.*—1 to 2 drachms (4 to 8 ml.).

Contains per drachm approximately 3 gr. each of sodium and potassium formates and  $1\frac{1}{2}$  m. of solution of strychnine hydrochloride, in simple elixir.

**Calcii Formas (B.P.C.).**  $(\text{H}\cdot\text{COO})_2\text{Ca} = 130\cdot1$ .

*Dose.*—3 to 10 grains (0·2 to 0·6 g.).

White crystals soluble 1 in 8 of water.

**Ferri Formas (B.P.C.).** *Syn.* FERRIC FORMATE.

$\text{Fe}_2(\text{OH})_2(\text{HCOO})_4\cdot 4\text{H}_2\text{O} = 588\cdot7$ .

*Dose.*—1 to 5 grains (0·06 to 0·3 g.).

Red crystals or powder soluble 1 in 18 of water forming an unstable solution, and 1 in 20 of dehydrated alcohol.

**Lithii Formas.**  $\text{H}\cdot\text{COOLi}\cdot\text{H}_2\text{O} = 69\cdot96$ .

*Dose.*—1 to 5 grains (0·06 to 0·3 g.). As much as  $1\frac{1}{2}$  g. of this salt have been given daily.

White crystalline powder freely soluble in water.

**Magnesium Formas.**  $(\text{H}\cdot\text{COO})_2\text{Mg}\cdot 2\text{H}_2\text{O} = 150\cdot4$ .

*Dose.*—3 to 10 grains (0·2 to 0·6 g.).

Colourless deliquescent crystals soluble in water.

**Potassii Formas (B.P.C.).**  $\text{H}\cdot\text{COOK} = 84\cdot11$ .

*Dose* and use similar to the sodium salt.

Crystalline hygroscopic powder very soluble in water forming neutral solution.

[P1-81] **Strychninae Formas.**

$\text{C}_{21}\text{H}_{22}\text{O}_2\text{N}_2$ ,  $\text{H}\cdot\text{COOH} = 380\cdot2$ .

*Dose.*— $\frac{1}{64}$  grain (0·001 g.), by hypodermic injection.

White crystalline powder, soluble in water about 1 in 5. A nerve stimulant and muscular tonic.

[P1] **Acidum Oxalicum (B.P.C.).**  $(\text{COOH})_2\cdot 2\text{H}_2\text{O} = 126\cdot0$ .

[P1] "*Oxalic acid.*"

[P2] "*Metallic oxalates.*"

[S3] "*Oxalic acid; metallic oxalates—in laundry blue; polishes.*"

White crystals soluble in water about 1 in 12; a powerful poison, made by acting on wood, sugar, starch, etc., with sodium hydroxides, or by heating sodium formate.

The toxicity of this acid in dilute solution and of its salts is due to their withdrawal of ionisable calcium from the blood and tissues. Strong solutions of the acid are poisonous by corrosive action. Toxic symptoms and cardiac depression can be relieved by giving soluble calcium salts.

**Antidotes.** Give immediately 2 dr. of chalk or magnesia mixed with water. Empty stomach, using cautiously a soft stomach tube with 4 oz. of magnesia in 2 gallons of water. Do *not* give hydroxides or carbonates of potassium, sodium or ammonium, as these form soluble oxalates. Give 1 oz. of castor

oil. Keep the patient warm. Saline infusion with dextrose for collapse.

Is used for removing ink stains and iron mould, cleaning leather, etc., and removing the colour from calico printing.

[P2] **Potassii Quadroxalas (B.P.C.)**. *Syn.* SAL ACETOSELLA, POTASSIUM TETROXALATE, SALT OF SORREL, SAL LIMONIS, SALTS OF LEMON.  $\text{KHC}_2\text{O}_4 \cdot \text{H}_2\text{C}_2\text{O}_4 \cdot 2\text{H}_2\text{O} = 254.1$ .

Colourless crystals soluble about 1 in 30 of cold water, 1 in 12 of hot water; slightly soluble in alcohol.

*Uses.* To remove rust and ink spots; in metal polishes.

[P2] **Potassii Binoxalas**. *Syn.* POTASSIUM ACID OXALATE.  $\text{KHC}_2\text{O}_4 \cdot 2\text{H}_2\text{O}$ . Formerly supplied as salts of lemon.

[P2] **Potassii Oxalas**, the neutral salt,  $\text{K}_2\text{C}_2\text{O}_4$ , is added to blood as an anti-coagulant.

[P2] **Cerii Oxalas (B.P.C., P. Jap. V)**.

*Dose.*—2 to 10 grains (0.12 to 0.6 g.), in powders or cachets.

A white or pinkish, granular, odourless and tasteless powder, obtained as a by-product in the separation of thorium from monazite, and consisting of about 50% of cerous oxalate,  $\text{Ce}_2(\text{C}_2\text{O}_4)_3 \cdot 10\text{H}_2\text{O} = 724.4$ , with the oxalates of numerous other rare earths especially lanthanum, praseodymium and neodymium.

*Insoluble* in water; soluble in warm, dilute acids. Used in chronic vomiting, especially that of pregnancy, also in chronic diarrhoea, hysteria, epilepsy and migraine.

[P2] **Cerocol (Coates & Cooper, London)**. Colloidal cerium oxalate in tablets containing 0.05 g. In vomiting, especially of pregnancy.

**Acidum Succinicum (B.P.C.)**.  $(\text{CH}_3\text{COOH})_2 = 118.09$ .

*Dose.*—5 to 10 grains (0.3 to 0.6 g.).

Obtained on destructive distillation of amber, or by fermentation of tartaric (dihydroxysuccinic) acid or malic acid, or as by-product in fermentation of sugar. Colourless crystals with very acid taste, soluble 1 in 20 of water, 1 in 9 of alcohol.

In 1937 Koranyi and Szent-Györgyi (*Dtsch. med. Wschr.*, 1937, 1029) advocated the use of succinic acid by the mouth in the treatment of diabetic ketosis. They claimed that the administration of 1 g. daily, in divided doses, in a 2% aqueous solution, kept the urine free from acetone bodies in cases where insulin had failed to control the symptoms. Other workers, including Lawrence (*Brit. med. J.*, ii/1937, 214), were unable to substantiate these claims.

**Asparagin**. *Syn.* ALTHEIN, AMINOSUCCINIC ACID AMIDE.

$\text{HOOC}(\text{NH}_2)\text{HC}(\text{CH}_3)\text{CONH}_2 \cdot \text{H}_2\text{O} = 150.1$ . *Dose.*—5 to 10 grains. White crystals, having a slightly acid reaction. Soluble 1 in 50 of water, also in acid and alkaline solutions. Insoluble in absolute alcohol and ether. An aqueous solution dissolves freshly precipitated mercuric oxide, and this has been used for hypodermic injection in syphilis. Has decided diuretic effect. For cardiac dropsy and chronic gout, 1 grain is given three times a day.

## ACIDUM GLYCEROPHOSPHORICUM

*B.P.C.*

$\text{C}_3\text{H}_5(\text{OH})_2\text{O} \cdot \text{PO}(\text{OH})_2 = 172.1$ .

*Syn.* GLYCERYLPHOSPHORIC ACID, MONOGLYCERYLPHOSPHORIC ACID.

*Dose.*—5 to 10 minims (0.3 to 0.6 ml.).

A dibasic acid prepared by heating glycerin with phosphoric acid *in vacuo*. Occurs as a colourless, odourless liquid containing the  $\alpha$  and  $\beta$  monoglycerides equivalent to about 20% *w/w* of  $C_4H_9O_6P$ . Sp. gr. 1.095 to 1.105. The chief constituent is the  $\alpha$  variety. The acid is readily decomposed into glycerin and phosphoric acid on heating.

Stronger solutions, namely, 25% (sp. gr. about 1.13) and 50% (sp. gr. about 1.30) are also obtainable.

**Uses of the Glycerophosphates.** Thought to aid metabolism, hence given in emaciation and generally for tonic action. The compound syrup and glycerin of glycerophosphates, the syrup of glycerophosphates with formates, and many of the milk and glycerophosphate preparations are claimed to have tonic properties in devitalised conditions, *e.g.*, during convalescence from illness.

The glycerophosphates were originally introduced into medicine by Robin, on the grounds that lecithin contains its phosphorus in the form of the glycerophosphoric radical.

**Calcii Glycerophosphas** (*B.P.C.*, *P. Dan.*, *Fr. Cx.*, *P. Belg. IV*, *P. Helv. V*, *P.G. VI*, and *P. Ital. V*). *Syn.* CALCIUM GLYCERINOPHOSPHORICUM (*P. Jap. V*), NEUROSINA (*F.E. VIII*).  $CaC_2H_5(OH)_2PO_4 \cdot 2H_2O = 246.2$ .

**Dose.**—3 to 10 grains (0.2 to 0.6 g.) or more *per os* in water, *vide infra*. *Hypodermically* 1 grain (0.06 g.) in 40 minims (2.5 ml.). *Intravenously* 1 grain (0.06 g.) in 100 minims (6 ml.) is suggested by analogy with the lactophosphate.

A white crystalline powder consisting mainly of the  $\alpha$ -glycerophosphate. The  $\beta$ -glycerophosphate is less soluble, and usually contains added citric acid to increase the solubility. Calcium glycerophosphate is formed, together with choline, on the breaking up of lecithin in the process of digestion.

**Soluble** about 1 in 40 of cold water, but different makers' products vary according to whether the compound is mainly the  $\alpha$  or the  $\beta$  modification. (The  $\alpha$  position is the terminal hydroxyl in glycerin and the  $\beta$  the central in combination with phosphoric acid.) It is only slightly soluble in hot water, soluble also in glycerin, insoluble in alcohol.

**Incompatible** with mineral acids and with soluble carbonates and phosphates. Solutions decompose when heated.

### Caseinum Glycerophosphaticum (*B.P.C.*).

**Dose.**—1 to 4 drachms (4 to 16 g.).

Soluble casein with  $2\frac{1}{2}\%$  each of sodium and calcium glycerophosphates.

**Glycolactophos** (*Roberts, London*), **Sanatogen** (*Genatosan, Loughborough*) and **Vitafer** (*Southall Bros. & Barclay, Birmingham*) are casein and glycerophosphate combinations used in neurasthenia, and enfeebled nervous conditions generally.

**Ferri Glycerophosphas** (*B.P.C.*). *Syn.* FERRIC GLYCEROPHOSPHATE.

**Dose.**—1 to 5 grains (0.06 to 0.3 g.). In yellow or greenish-yellow scales containing 13 to 16% of Fe, together with alkali citrate. Slowly soluble in water.

**Magnesi Glycerophosphas (B.P.C.).** $\text{MgC}_2\text{H}_3(\text{OH})_2\text{PO}_4 \cdot 2\text{H}_2\text{O} = 230.4$ .

*Dose.*—5 to 10 grains (0.3 to 0.6 g.). A white amorphous powder, soluble 1 in about 50 of water. May be rendered more soluble by addition of citric acid or alkali citrate.

**Mangani Glycerophosphas.  $\text{MnC}_2\text{H}_4(\text{OH})_2\text{PO}_4 = 225.0$ .**

*Dose.*—1 to 5 grains (0.06 to 0.3 g.). Pinkish amorphous powder, only slightly soluble in water. The relative anæmia which is often associated with cardiac overstrain has been treated by administering manganese glycerophosphate with hæmoglobin.

**Potassii Glycerophosphas Liquidus (B.P.C.).***Dose.*—10 to 30 grains (0.6 to 2 g.).

A colourless syrupy liquid containing about 50% *w/w* of the hydrated neutral potassium salts of  $\alpha$ - and  $\beta$ -glycerophosphoric acids, calculated as  $\text{C}_2\text{H}_7\text{O}_3 \cdot \text{PO}_3\text{K}_2 \cdot 3\text{H}_2\text{O} = 302.3$ . A 75% solution is also obtainable.

**Quinina Glycerophosphas (B.P.C.).** $(\text{C}_{20}\text{H}_{24}\text{O}_2\text{N}_2)_2 \cdot \text{C}_2\text{H}_4\text{O}_3\text{P} \cdot 4\text{H}_2\text{O} = 892.96$ .

*Dose.*—1 to 10 grains (0.06 to 0.6 g.). *Fr. Cx.* has the compound with  $5\text{H}_2\text{O}$ , termed "basic" quinine glycerophosphate. White crystalline powder, soluble 1 in about 200 of water, and 1 in 40 of alcohol 90%.

**Sodii Glycerophosphas (B.P.C., *P. Ned. V.*). *Syn.* SODIUM GLYCERYLPHOSPHATE.  $\text{C}_2\text{H}_7\text{O}_3\text{PNa}_2 \cdot 5\frac{1}{2}\text{H}_2\text{O} = 315.2$ . *P. Ital. V, P. Dan., P. Belg. IV and F.E. VIII* have  $5\text{H}_2\text{O}$ .**

*Dose.*—5 to 10 grains (0.3 to 0.6 g.), *per os*; also given *hypodermically* in 3 to 5 grain doses.

In crystalline masses or as a white powder, consisting of the  $\beta$ -glycerophosphate. *Fr. Cx.* describes it as a variable mixture of  $\alpha$ - (with  $5\text{H}_2\text{O}$ ) and  $\beta$ -glycerophosphates (with  $6\text{H}_2\text{O}$ ).

**Soluble** 1 in 4 of water.

**Sodii Glycerophosphas Liquidus (B.P.C.).***Dose.*—10 to 30 grains (0.6 to 2 g.).

A colourless or faintly yellow syrupy liquid consisting of a 50% *w/w* solution of the sodium salts of  $\alpha$ - and  $\beta$ -glycerophosphoric acids. A 75% *w/w* solution is also obtainable in commerce.

**[P1-S1] Strychnina Glycerophosphas.**

*Dose.*— $\frac{1}{2}$  to  $\frac{1}{10}$  grain (0.001 to 0.003 g.). White crystalline powder, soluble in water.

**[P1] Metastone (Parke, Davis, London).** Glycerophosphates of strychnine ( $\frac{1}{100}$  gr. per dr.), calcium, potassium, sodium, manganese with vitamin B extract etc. *Dose.*—1 to 2 drachms before and after meals. Tonic and restorative.

**Emulsio Olei Morrhua cum Glycerophosphatibus (B.P.C.).***Dose.*— $\frac{1}{4}$  to 1 ounce (8 to 30 ml.).

Contains 50% *v/v* of cod-liver oil with the glycerophosphates of calcium, magnesium, iron, sodium and potassium.

**Emulsio Paraffini Liquidi cum Glycerophosphatibus (B.P.C.). *Syn.* EMULSIO PETROLEI CUM GLYCEROPHOSPHATIBUS.***Dose.*—1 to 4 drachms (4 to 16 ml.).

Contains 50% *v/v* of liquid paraffin with the glycerophosphates of calcium, magnesium, iron, sodium and potassium.



**Extractum Malti Liquidum cum Glycerophosphatibus** (B.P.C.).

*Dose.*—1 to 4 drachms (4 to 16 ml.).

Contains in 1 dr. the equivalent of  $\frac{1}{2}$  gr. each of potassium and sodium glycerophosphates, in liquid extract of malt.

**Glycerinum Glycerophosphatum Compositum** (B.P.C.).

*Syn.* ELIXIR GLYCEROPHOSPHATUM, GLYCEROL GLYCEROPHOSPHATIS.

*Dose.*—1 to 2 drachms (4 to 8 ml.).

Contains in 1 dr. calcium glycerophosphate  $1\frac{1}{2}$  gr., potassium, sodium, and magnesium glycerophosphates of each about  $\frac{1}{2}$  gr., and iron glycerophosphate about  $\frac{1}{4}$  gr. It contains no sugar or strychnine.

**Glycerinum Glycerophosphatum cum Medulla Rubra** (B.P.C.).  
*Syn.* GLYCEROL GLYCEROPHOSPHATIS CUM MEDULLA RUBRA, ELIXIR GLYCEROPHOSPHATUM CUM MEDULLA RUBRA.

*Dose.*—1 to 2 drachms (4 to 8 ml.).

Equal parts of compound glycerin of glycerophosphates and extract of red bone marrow.

**[P1] Syrupus Glycerophosphatum Compositus** (B.P.C.).

*Syn.* SYRUPUS GLYCEROPHOSPHATUM RUBER.

*Dose.*—1 to 2 drachms (4 to 8 ml.).

Contains the glycerophosphates of calcium, sodium, potassium, magnesium and iron, with about  $\frac{1}{10}$  gr. of strychnine and  $\frac{1}{2}$  gr. of caffeine per drachm.

**Syrupus Glycerophosphatum Compositus cum Medulla Rubra** (B.P.C.).

*Dose.*—1 to 2 drachms (4 to 8 ml.).

Equal parts of compound syrup of glycerophosphates and extract of red bone marrow.

**[P1] Syrupus Glycerophosphatum cum Formatibus** (B.P.C.). *Syn.* COMPOUND ELIXIR OF GLYCEROPHOSPHATES WITH FORMATES.

*Dose.*—1 to 2 drachms (4 to 8 ml.).

Contains the glycerophosphates of calcium, sodium, potassium, magnesium and iron, with about  $\frac{1}{10}$  gr. of strychnine and 3 gr. each of potassium and sodium formates per drachm.

**[P1] Syrupus Glycerophosphatum et Pepsini Compositus** (B.P.C.).

*Syn.* SYRUPUS GLYCEROPHOSPHATUM COMPOSITUS (Robin).

*Dose.*—1 to 2 drachms (4 to 8 ml.).

Contains the glycerophosphates of calcium, sodium, potassium, magnesium and iron, with about  $\frac{1}{2}$  gr. of pepsin and 2 m. of tincture of ignatia per drachm.

**Syrupus Glycerophosphatum Flavus** (B.P.C.).

*Dose.*—1 to 2 drachms (4 to 8 ml.).

Is of the same strength as Syr. Glycerophosph. Co., but contains no strychnine, and is coloured yellow.

## ACIDUM HYDRIODICUM DILUTUM

(with METALLIC IODIDES)

*B.P.C., U.S.P. XI.*

*Dose.*—5 to 10 minims (0.3 to 0.6 ml.) well diluted, or in syrup.  
*U.S.P.* average dose 15 minims.

This acid is prepared by heating red phosphorus and iodine in presence of water, or by the action of hydrogen sulphide on a solution of iodine.

A colourless, odourless liquid containing 10% *w/w* of HI with 1% *w/w* of  $H_3PO_2$  added to prevent discoloration on keeping. Other strengths available in commerce are 20% with sp. gr. 1.17, 46 to 47% with sp. gr. 1.5, and the constant boiling acid containing 57% *w/w* and boiling at 125°.

**Syrupus Acidi Hydriodici (B.P.C.).**

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.), well diluted.

Dilute hydriodic acid 10% *v/v*, with distilled water and syrup.

**Syrupus Acidi Hydriodici (U.S.P. XI).**

*Average dose.*—60 minims (4 ml.).

Diluted hydriodic acid (10%) 14 ml., sucrose 45 g., water to 100 ml.

**Ammonii Iodidum (B.P.C., P. Helv. V).  $NH_4I=145.0$ .**

*Dose.*—2 to 6 grains (0.12 to 0.4 g.).

White, deliquescent, crystalline granules becoming yellow on exposure to air, owing to loss of ammonia and liberation of iodine.

**Soluble** 1 in 1 of water, 1 in 3 of alcohol 90%, 3 in 4 of glycerin.

It causes less depression than potassium iodide, and is preferred by some for syphilis and rheumatism.

**Calcii Iodidum (B.P.C.).  $CaI_2=293.9$ . Prop. Name. CALCIDIN (Abbott Laboratories, London), available in tablets.**

*Dose.*—1 to 5 grains (0.06 to 0.3 g.). Given in dilute aqueous solution.

Deliquescent crystalline powder. On exposure to light or air will liberate iodine; best preserved in amber bottles.

**Uses.** May be given internally in place of potassium iodide. A 6 to 12% ointment is said to be of value in the treatment of glandular swellings, foul ulcers, and chilblains.

[P1-S1-S4] **Calcidrine Syrup (Abbott Laboratories, London).** Contains calcium iodide 7 gr., ephedrine hydrochloride  $\frac{1}{2}$  gr., codeine sulphate  $\frac{1}{2}$  gr., Nembutal  $\frac{1}{2}$  gr., syrup of wild cherry and syrup of tolu to 1 oz. Antispasmodic and sedative cough syrup.

[P1] **Foille (Carbisulphoil Co., Dallas; Anglo-French Drug Co., London).** Emulsion of vegetable oil containing potassium iodide 0.14%, calcium iodide 0.25%, calcium thiosulphate 0.02%, calcium soap 0.39%, calcium sulphite 0.086%, oxyquinoline sulphate 0.1%, ethyl alcohol 1.4%, phenol 2.8%, benzocaine 1.3%, water 3.4%, vegetable oil 90.114%, with traces of sulphur and glycerin. Advocated for the treatment of burns, being applied with a brush, and the area then covered with gauze soaked in the preparation. The application is renewed thrice daily at first, the whole area being cleansed after 45 hours. The preparation is also used for indolent ulcers, etc., and for some mycotic infections.

**Lithii Iodidum (B.P.C.).  $LiI=133.9$ .**

*Dose.*—1 to 5 grains (0.06 to 0.3 g.).

White crystalline deliquescent powder becoming yellowish when stored. Contains theoretically 94.7% of I.

**Soluble** in water and alcohol 90%.

An antiarthritic, and has been employed in syphilis.

**Potassii Iodidum** (B.P., U.S.P. XI, Fr. Cx., P. Dan.).

KI=166.0.

*Dose*.—5 to 30 grains (0.3 to 2 g.)—often much increased, even up to 4 drachms per day. U.S.P. XI average dose 5 grains; as antiluetic 30 grains.

(**Kalium Jodatum** (P.G. VI, P. Helv. V, P. Jap. V) is potassium iodide. Potassium iodate,  $KIO_3$ , is called **Kalium Jodicum** in Germany.)

In white cubic crystals or granular powder *soluble* 1 in 0.7 of water, 1 in 12 of alcohol 90%, 1 in 75 of acetone, 1 in 5 of methyl alcohol, and 1 in 2 of glycerin.

Solutions become yellowish in colour on standing, especially when exposed to light, owing to the liberation of a trace of free iodine. A slightly alkaline solution keeps better than an acid one.

**Incompatible** in solution with Spiritus Ætheris Nitrosi (unless made alkaline), salts of iron (except Ferri et Ammonii Citras and Liquor Ferri Acetatis), salts of bismuth, lead and mercury, Liquor Strychninæ Hydrochloridi, quinine sulphate and other alkaloidal salts, and with silver nitrate and potassium chlorate.

**Uses.** In universal use in the later stages of syphilis, in arteriosclerosis and in certain cases of gout and rheumatism. In rheumatoid arthritis may be given in conjunction with guaiacol carbonate. Small doses are valuable in the early stages of bronchitis, rendering the secretion less viscid. It also assists tuberculous expectoration. Is useful in conjunction with creosote in lobar pneumonia.

For actinomycosis it is specific; very large doses are given. Sporotrichosis and blastomycosis also respond. Acute parotitis is favourably treated with iodine externally and potassium iodide internally. In tinnitus aurium associated especially with vertigo, due to labyrinthine disease, full doses may be given. Is of value also in lymphangitis.

In aneurysm moderate to full doses are given. The addition of ammonium bromide is often useful.

In 5 to 15 grain doses twice or thrice daily, often with tincture of stramonium, is useful in asthma, both during the paroxysms and in the interval.

In arteriosclerosis 3 to 5 grain doses thrice daily with potassium bicarbonate 5 to 10 grains, sal volatile 20 minims, and an ounce of gentian infusion continued for four months at a time with interruptions of 10 or 12 days.

In areas where goitre is endemic, potassium iodide is administered prophylactically, but care must be taken to avoid overdosage and consequent hyperthyroidism. For this purpose it may be taken as *iodised table salt* containing about 1 in 200,000 of potassium or sodium iodide.

An assessment of the expectorant properties of potassium iodide and ipecacuanha, conducted under controlled conditions on 17 consecutive cases of chronic bronchitis, showed that the output of sputum was unchanged by the use of these drugs.—S. Alstead, *Lancet*, ii/1939, 932.

**CARDIO-VASCULAR SYPHILIS.** Potassium iodide the most efficacious treatment, though explanation of its action is difficult. Iodine by inunction may be substituted. Mercury is not more effective than arsenic, but safer. 0.3 g. of nearsphenamine at intervals of a week over long periods, till 5 g. have been taken. Iodide and mercury continuous, and a course of organic arsenic added from time to time.—Carey F. Coombs, *Brit. med. J.*, ii/1930, 893.

**GOITRE.** The Swiss Goitre Commission (1922) after exhaustive investigations fixed the maximum amount as 1 part iodine in 200,000 parts of salt. This is the amount adopted in this country. Marine in the U.S.A. advises 1 in 500 in mildly goitrous districts.—J. A. Goodfellow, *Brit. med. J.*, i/1925, 331.

Iodine stimulates intestinal movements and in excessive doses causes diarrhoea. By the mouth potassium iodide causes a rapid rise in the iodine content of the blood. It is only in exceedingly high dosage that iodine causes injury to the sex glands—no injurious effects occur with small or moderate dosage. In the human subject the minimum amount of iodine required daily for an adult male is calculated at 15 microgrammes (millionths of a gramme). The dosage necessary to prevent goitre is higher, and the lower physiological limit is placed at about 100 microgrammes per day.—*Spec. Rep. Ser. med. Res. Coun., Lond.*, No. 123, 1929.

**GUMMA.** The action of potassium iodide in promoting the absorption of a gumma is so specific and so rapid that it is sometimes used diagnostically. The usual starting dose is 15 gr. three times a day in a simple mixture which may be increased up to 60 gr. three times daily.—H. K. Goadby, *Practitioner*, ii/1939, 654.

**LEPROSY.** Extremely useful in the last stages of recovery, but should only be used in patients maintaining a high resistance and tolerating full doses of Hydnocarpus esters.—E. Muir, *Trans. R. Soc. trop. Med. Hyg.*, 1931, 94.

**TONSILLITIS.** The administration of small doses of potassium iodide over a period of 3 months, 1 to 3 gr. once a day according to the age of the child, is a valuable form of conservative treatment for enlarged tonsils and adenoids. 70% of cases may be successfully treated by this method.—P. W. Leathart, *Brit. med. J.*, ii/1938, 835.

**Toxic Effects.** Idiosyncrasy to iodides sometimes occurs, comparatively small doses producing nasal catarrh, lachrymation, skin rashes and headache.

### **Linimentum Potassii Iodidi (B.P.C.).**

A fluid liniment containing potassium iodide 1 in 10.

### **Linimentum Potassii Iodidi cum Sapone (B.P.C.).**

A solid liniment containing potassium iodide about 1 in 7 with curd soap, glycerin, oil of lemon and water.

**Mist. Pot. Iod. (N.I.F.).** Potassium iodide 2½ gr., ammonium carbonate 2½ gr., concentrated compound infusion of gentian 15 m., chloroform water to ½ oz.

[P2] **Mist. Pot. Iod. et Arsen. (N.I.F.).** Potassium iodide 5 gr., arsenical solution 3 m., concentrated infusion of calumba 30 m., water to ½ oz.

**Mist. Pot. Iod. c. Ipecac. (N.I.F.).** Potassium iodide 5 gr., tincture of ipecacuanha 5 m., glycerin 20 m., water to ½ oz.

### **Unguentum Potassii Iodidi (B.P.C.).**

10% with potassium carbonate in water and benzoated lard.

[P1] **Mixed Treatment Tablets (Parke, Davis, London).** Potassium iodide 2 gr., syrup of ferrous iodide 5 m., mercuric chloride ½ gr., solution of arsenous and mercuric iodides 2 m., tincture of nux vomica 4 m.

*Dose.*—1 to 3 tablets. Syphilis, tabes, etc.

**Sodii Iodidum (B.P., U.S.P.XI, Fr. Cx., P. Dan.).** NaI=149.92.

*Dose.*—5 to 30 grains (0.3 to 2 g.). U.S.P. XI average dose 5 grains.

(**Natrium Jodatum**, *P. Helv. V, P.G., P. Jap. V*, is sodium iodide. Sodium iodate is called **Natrium Jodicum** in Germany.)

A white crystalline deliquescent powder, **soluble** 3 in 2 of water, 1 in 3 of alcohol 90%, and in glycerin and acetone. Must be crystallised at a temperature above 20° otherwise the hydrated salt with 2H<sub>2</sub>O is obtained.

**Uses** and incompatibilities are in general similar to those of the potassium salt, *q.v.*

Intravenous injections of a 10% solution have been employed for their analgesic effect in various painful conditions, *e.g.*, herpes zoster, neuritis, sciatica, etc.

Of ten agents considered to be of value in clinical or experimental hyperthyroidism (sodium fluoride, vitamins A and D, vitamins B and G, sodium iodide, estrogenic hormones, ergotamine tartrate, quinine hydrochloride, vitamin C and sodium thiocyanate) only one, namely, sodium iodide was found to limit the increased metabolic weight induced in guinea-pigs by thyrotrophic extracts. It is doubted therefore whether any of the other agents have any therapeutic value in clinical hyperthyroidism.—W. C. Cutting and G. B. Robson, *J. Pharmacol.*, 1939, 66, 389.

**GOITRE** well treated by six intravenous injections on alternate days of 6 gr. in 5 ml. water.—Reddi, *Prescriber*, 1928, 159.

**HERPES ZOSTER.** Intravenous injection of sodium iodide 20 ml. of 10% solution on the 1st, 2nd, 4th and 7th days (some patients less); also a dusting powder of zinc oxide, camphor, starch and morphine. All cases cleared up in less than 17 days.—*Prescriber*, 1931, 352.

The intravenous injection of sodium iodide is a specific for herpes zoster. A dose of 2 g. is given every other day and never more than four doses are necessary.—N. T. Beers, *J. Amer. med. Ass.*, i/1939, 2552.

**PARESIS.** *Usual dose.*—1 g. in 10 ml. of water. Doses of 100 ml. of 10% solution generally well tolerated at 4 to 7-day intervals. Give preliminary test dose of 20 ml. As much as 30 to 50 g. has been injected in one dose.—*J. Amer. med. Ass.*, ii/1929, 1753.

### **Sodium Iodide as Pyelographic Medium.**

**U.C.H.** has a sterile solution of sodium iodide 15 g. in distilled water to 50 ml.

**PYELOGRAPHY.** 13.5% sodium iodide is best. Renal function and pyelography are mutually interdependent.—*Lancet*, i/1929, 1160.

Prolonged anuria in a woman following injection of sodium iodide 15% into pelvis for pyelography. Relieved by venesection.—D. D. Pinnock and I. W. Matthews, *Lancet*, ii/1931, 529.

For further details see Vol. II under X-ray diagnosis.

**Na iodine** (*Anglo-French Drug Co., London*). A stabilised 1% solution of sodium iodide for injection. *Dose.*—10 ml. intramuscularly. For the relief of pain in all types of neuralgia and neuritis. **Vitamised Na iodine 'A'** contains 2 mg. of crystalline vitamin B<sub>1</sub> in each 10 ml. ampoule, and 'B' contains 1 cg. of vitamin B<sub>1</sub> in each 10 ml. ampoule; these are for the treatment of neuritis by intramuscular injection.

**Thionaiodine** (*Anglo-French Drug Co., London*). A stabilised solution of sodium iodide and magnesium tetrathionate available in two forms suitable for intramuscular and intravenous injection respectively. Advocated as an analgesic and sedative in all painful conditions such as sciatica, rheumatism, etc.

*Dose.*—Intramuscularly, or intravenously, 5-20 ml. daily.

### **Strontii Iodidum (B.P.C.).** SrI<sub>2</sub>·6H<sub>2</sub>O=449.6.

*Dose.*—5 to 15 grains (0.3 to 1 g.).

In deliquescent crystalline masses, with bitter saline taste.

**Soluble** 2 in 1 of water, and in alcohol.

Exophthalmic goitre of children has been treated with this and the bromide, also asthma, rheumatism, and chronic endocarditis.

**Zinci Iodidum** (*B.P.C.*).  $\text{ZnI}_2 = 319.2$ .

*Dose.*— $\frac{1}{2}$  to 2 grains (0.03 to 0.12 g.).

A white deliquescent powder turning brown on exposure. For cerebral, spinal, and nervous diseases in the third stage of syphilis, and in epilepsy, but rarely used.

**Talbot's Solution** (*Canad. Form.*). Zinc iodide 110 gr., distilled water 82 m., iodine 183 gr., glycerin to 1 oz.

**Acidum Iodicum**.  $\text{HIO}_3 = 175.9$ .

*Dose.*—1 to 5 grains (0.06 to 0.3 g.).

White crystalline powder very soluble in water. It is employed in ozæna, for deodorising offensive urine, as an irrigant in empyema (strength 1 in 500) and for leg ulcers, as a mouth-wash, *e.g.*, in inoperable epithelioma, and as a throat swabbing in diphtheria. Internally a drachm of a 1 in 100 solution, well diluted, has been given in gastro-intestinal sepsis, as in typhoid fever. The calcium salt is principally employed.

**Calci Iodas**. *Syn. CALCINOL*.  $\text{Ca}(\text{IO}_3)_2, 6\text{H}_2\text{O} = 498.0$ .

*Dose.*—3 to 4 grains 3 times daily in solution.

Tasteless, odourless powder, soluble in 380 parts of water at 11.5°. Acts equally well in an acid or alkaline medium as a deodorant and anti-putrefactive.

**Sodii Iodas**.  $\text{NaIO}_3 = 197.9$ . White, crystalline powder, soluble 1 in 10 of water; insoluble in alcohol. Used as a dusting powder with 8 parts of boric acid, or as a saturated aqueous solution as a dressing for ulcers.  $1\frac{1}{2}$  grains in 5% solution has been injected for acute and chronic articular rheumatism.

## ACIDUM HYDROBROMICUM

(with METALLIC BROMIDES)

*B.P.C.*

$\text{HBr} = 80.92$ .

Hydrobromic acid of sp. gr. 1.303 to 1.314 and containing about 34.5% *w/w* of  $\text{HBr}$ . Liquid with an acid smell. Should not be exposed to sunlight. It may be prepared by the action of bromine on amorphous phosphorus in the presence of water and is colourless or straw-coloured. Commercially the acid is also obtainable in the following strengths—25% *w/w* (sp. gr. 1.208), 30% *w/w* (sp. gr. 1.260), and 40% *w/w* (sp. gr. 1.375). *P. Ned.* is 4N (about 32%).

**Acidum Hydrobromicum Dilutum** (*B.P., P. Helv. V.*).

*Dose.*—15 to 60 minims (1 to 4 ml.); 60 minims = 10 grains of potassium bromide approximately. Contains 10% *w/w* of  $\text{HBr}$ . Sp. gr. 1.072 to 1.075. An acid of approximately the same strength is obtained by diluting 290 g. of the concentrated acid with 710 g. of water (approximately 4 fl. oz. 6 fl. dr. to 20 fl. oz.).

*Uses.* To allay nervous excitability and exhaustion, and as an alternative to potassium bromide; given with morphine to allay after-effects. As a solvent for quinine and to prevent quinism 8 minims will dissolve 5 grains of quinine sulphate in water. Obviates the sense of fullness of the head felt when taking iron. It is useful for tinnitus aurium and tickling hacking cough in

doses of 10 minims, and in headache, with flushing of the face and ringing in the ears. In vertigo it is successful and it relieves toothache. In epilepsy, up to  $\frac{1}{2}$  ounce well diluted may be given, even to 3 ounces daily. It is also used with quinine hydrobromide in the treatment of primary Graves' disease.

[P1] **Mistura Chloroformi Composita** (B.P.C.). *Syn.* MISTURA TUSSI SEDATIVA, MISTURA TUSSI RUBRA.

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Contains 15 m. of dilute hydrobromic acid and  $\frac{3}{10}$  gr. of morphine hydrochloride per drachm.

**Ammonii Bromidum** (B.P.C., U.S.P. XI, *Fr. Cx.*, *P. Jap. V*, *P. Helv. V*, *P. Dan.*).  $\text{NH}_4\text{Br} = 97.96$ .

*Dose.*—5 to 30 grains (0.3 to 2 g.).

Small colourless crystals. *Soluble* 2 in 3 of water, 1 in 13 of alcohol 90%. *Incompatible* with mineral acids, silver nitrate and spirit of nitrous ether.

*Uses.* Possesses similar sedative properties to those of the other bromides (*vide* Potassii Bromidum) and is thought to cause less depression.

In sea sickness ammonium bromide, beginning a day or so before the voyage, in doses of 20 gr. in chloroform water with 15 gr. of sodium bicarbonate thrice a day, has been found useful.

In tinnitus a course of ammonium bromide with compound syrup of glycerophosphates is said to be of value, the bromide being taken on retiring.

**Pastilli Ammonii Bromidi** (B.P.C.) contain 1 gr. (0.06 g.).

**Tabellæ Ammonii Bromidi** (B.P.C.) contain 5 gr. (0.3 g.).

**Ammonii Bromidum Effervescens** (B.P.C.).

*Dose.*—75 grains to 1 ounce (5 to 30 g.). 1 in 12 $\frac{1}{2}$ .

**Mistura Ammonii Bromidi, Phenazoni et Caffeinæ.**

*Dose.*—1 ounce (30 ml.), repeated in two hours if necessary.

Ammonium bromide 10 gr., phenazone 10 gr., caffeine citrate 5 gr., chloroform water to 1 oz. Ordinary headache is rapidly relieved by this.

**Calcii Bromidum** (B.P.C., U.S.P. XI, *P. Helv. V*, *P. Dan.*, *P. Ned. V Supp. II*).  $\text{CaBr}_2 \cdot 2\text{H}_2\text{O} = 235.9$ .

*Dose.*—8 to 30 grains (0.5 to 2 g.).

A very deliquescent white crystalline powder with saline, bitter taste.

*Soluble* 1 in 0.3 of water and 1 in 0.6 of alcohol 10%.

When the aqueous solution is recrystallised the salt  $\text{CaBr}_2 \cdot 6\text{H}_2\text{O}$  is obtained. It is converted into  $\text{CaBr}_2 \cdot 2\text{H}_2\text{O}$  by heating to 180°.

*Fr. Cx.* obtains by melting  $\text{CaBr}_2 \cdot 2\text{H}_2\text{O}$  and allowing to solidify in its own water of crystallisation.

*Uses.* Is effective in epilepsy and sometimes preferred to potassium bromide.

**Syrupus Calcii Bromidi** (*Fr. Cx.*). Calcium bromide 25 g., water 15 g., orange-flower syrup 100 g., simple syrup 860 g.

**Calcibronat** (*Sandoz, London*). Calcium brom-lactobionate. Issued in granules and effervescent tablets, and in 5 and 10 ml. ampoules for intravenous or intramuscular injection.

A stable non-hygroscopic substance first produced by the National Bureau of Standards of the U.S. Department of Commerce. It is stated to have a sedative action almost twice that corresponding to its bromine content and not to cause bromide rashes. It contains 7.5% of Ca and 15% of Br, and is best prepared electrically from calcium carbonate, lactose and bromine.—(See H. S. Isbell, *J. Res. Nat. Bureau of Standards*, 1936, 331.)

**Lithii Bromidum (B.P.C.).** LiBr = 86.86.

*Dose.*—5 to 15 grains (0.3 to 1 g.).

White, deliquescent, slightly bitter granules, with neutral reaction. Contains a variable amount of moisture, but less than one molecule.

*Soluble* 5 in 3 of water; readily soluble in alcohol 90%.

Contains 91% of bromine as against 67% in potassium bromide; hence effect is greater, especially as a hypnotic, and in epilepsy.

**Magnesii Bromidum (B.P.C.).**  $MgBr_2 \cdot 6H_2O$  = 292.2.

*Dose.*—5 to 20 grains (0.3 to 1.2 g.).

Contains 54.9% of bromine. Given in hysteria and epilepsy as a nervine sedative. Soluble 1 in 0.6 of water and 1 in 2 of alcohol 90%.

**Potassii Bromidum (B.P., U.S.P. XI, Fr. Cx., P. Jap. V, P. Dan.).** KBr = 119.0.

*Dose.*—5 to 30 grains (0.3 to 2 g.). U.S.P. XI average dose 15 grains.

(**Kalium Bromatum** (P.G., P. Helv. V, P. Hung.) is potassium bromide. Potassium bromate,  $KBrO_3$ , is called **Kalium Bromicum** in Germany.)

Colourless or white crystals with saline taste. *Soluble* 1 in about 2 of water, and 1 in about 200 of alcohol 90%.

*Incompatible* with mineral acids, mercury and silver salts.

**Toxic Effects.** Prolonged administration may cause symptoms of bromism, including nausea, dullness and muscular weakness with acneiform or erythematous rashes. To avoid the onset give arsenical solution together with purgatives and salol. Patients saturated with bromides exhibit anæsthesia of the palate—a little known but useful diagnostic. Tickling the palate with a feather is a good means of eliciting the information. The effect of bromides is enhanced by adding potassium bicarbonate in doses equal to about a quarter of the total bromide given.

**BROMISM.** The early symptoms of bromide intoxication are an exaggeration of the therapeutic sedative effect. Definite retardation of thought, speech, and action appears, with anorexia, constipation, weakness and drowsiness. This stage is seldom dangerous if recognised before the appearance of frank psychosis; and the symptoms clear up gradually when the bromide is discontinued. If the drug continues to accumulate, outspoken psychosis frequently occurs. Drowsiness and lethargy may be replaced by insomnia and irritable restlessness. The patient refuses food and fluids, and may become severely dehydrated. Dry mucous membranes, furred tongue, foul breath, dilated pupils, ataxia and tremulousness are typical symptoms of the more severe states. Symptomatic or delirious psychotic manifestations appear. In some cases, skin lesions appear, but the skin may be normal in the presence of outspoken mental disturbance. Dependence upon the bromide eruption as a diagnostic aid is one of the chief reasons why symptomatic psychosis due to bromide pass unrecognised. A blood bromide level of 250 mg. per cent. or higher will account for a delirious psychosis in a patient who is in fairly good physical condition.—P. W. Preu, J. Romano and W. T. Brown, *New Engl. J. Med.*, 1936, 214, 57.



Levels of blood bromide under 100 mg. per cent. may generally be ignored; symptoms are likely to appear in elderly patients or in those with impaired cardiovascular or renal efficiency when the amount is between 100 and 200 mg. per cent.; levels above 200 mg. produce symptoms in most cases. It is rare for a blood bromide above 300 mg. to be tolerated without ill effect.—R. F. Barbour, F. Pilkington and W. Sargent, *Brit. med. J.*, ii/1936, 957.

There is no uniform threshold at which symptoms appear. Most authors consider that they do not appear until a level of 225 to 250 mg. is reached. This is definitely too high and in certain people a level of 150 mg. is quite sufficient to produce a definite degree of toxicity—cases have been reported when the level was below 125. The average dose of bromide prescribed is 15 to 20 grains thrice daily, and this figure is satisfactory when the patient is taking a normal diet containing 10 to 15 gr. of sodium chloride a day. If, however, the chloride intake diminishes, then the toxic level may be reached very rapidly. In order to **remove the bromide** from the tissues of a patient, the administration of bromide is stopped, sodium chloride 30 gr. thrice daily is given and fluids are given freely. It usually takes from 10 days to two weeks for the acute symptoms to clear up but often considerably longer before all evidence of toxæmia disappears.—R. F. Barbour, *Proc. R. Soc. Med.*, 1936, 29, 1391.

The blood bromides of 32 chronic epileptic psychotic patients were estimated, and although comparatively high levels were found in many cases no obvious instances of true bromide intoxication showing delirious or confusional reactions were discovered, though some of the patients had been taking 90 grains of bromide a day for ten years. Reduction in the bromide level produced no appreciable change in the mental state and no marked increase in the number of fits, which were definitely reduced in eight cases.—L. Minski and J. B. Gillen, *Brit. med. J.*, ii/1937, 850.

Report of a number of cases of bromide intoxication with a description of the physical and mental effects. Bromide intoxication itself can cause impairment of kidney function, the majority of cases showing a raised blood urea nitrogen which fell when the intoxication disappeared.—H. Tod and H. Stalker, *Edinb. med. J.*, 1938, 561.

Whereas the use of sodium chloride in bromide intoxication necessitates from 2 to 6 weeks of treatment, with *gastric aspiration* the bromides are eliminated in from 2 to 7 days. A continuous drainage with negative pressure bottles is simple and efficacious. Twelve cases of bromide psychosis so treated with gratifying results.—F. Lemere, *J. Amer. med. Ass.*, ii/1939, 1243.

**Uses.** Hypnotic and sedative. Much used in epilepsy, greatly reducing the number of fits. In recent epilepsy it should be given for a long period (not less than two years). If no benefit from 45 to 75 grains *per diem* some other remedy should be tried.

The following mixture has been recommended:—Potassium bromide 1 oz., potassium iodide 2 dr., ammonium bromide 3 dr., ammonium carbonate 1 dr., tincture of calumba 1 oz., water to 6 oz. One teaspoonful before each meal and three teaspoonfuls at bedtime. If petit mal exists alone, or co-exists with complete epilepsy, the dose of ammonium bromide must be increased and that of the other diminished.

Valuable especially in combination with chloral hydrate, in insomnia due to worry or overwork but not to pain. Large doses have been given in tetanus, and it has also been used as an antidote to strychnine poisoning. Sedative in spermatorrhœa and nymphomania. For gonorrhœal erections 15 to 35 gr. may be given 2 to 4 times daily in a cachet with lupulin 1 to 2 gr. and camphor 1 to 2 gr.

Bromide must not be administered over any prolonged period unless an adequate intake of fluids and chloride is maintained; and the physician should be constantly alert for symptoms of bromide intoxication. Bromide should not be employed in states of severe excitement and agitation because it is not effective unless dangerously large doses are given. Bromide should never be

used in cases of delirium due to either toxic or infectious causes. It should be used with caution in cases of arteriosclerosis, since delirium is readily produced if cerebral arteriosclerosis is present. Nephritis is a definite contraindication to the use of the drug. Bromide should not be used in cases of dehydration or severe malnutrition, in which the body fluids and chlorides are low.—P. W. Preu, J. Romano and W. T. Brown, *New Engl. J. Med.*, 1936, 214, 61.

**LABOUR.** A combination of potassium bromide and chloral hydrate is a safe and useful sedative in the first stage of labour, especially in excitable and nervous patients, and does not appear to lessen uterine contractions. Initial dose, 30 gr. of each drug, repeated in smaller doses at 3 or 4-hourly intervals. Vomiting avoided by sipping the mixture dissolved in at least 6 ounces of water with glucose and lemon juice.—L. McIlroy and H. Rodway, *J. Obstet. Gynec.*, 1933, 1175.

**Enema Potassii Bromidi (B.P.C.).**

*Dose.*—5 ounces (150 ml.).

Potassium bromide 1% w/v, acetylsalicylic acid 0.5% w/v and mucilage of tragacanth in normal saline.

**[P1] Mistura Bromidi Composita (B.P.C.).**

*Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.).

1 oz. contains 10 gr. each of the bromides of ammonium, potassium and sodium, and 10 m. of tincture of nux vomica.

**[P1] Mist. Brom. et Chloral. (N.I.F.).** Chloral hydrate 5 gr., potassium bromide 10 gr., liquid extract of hyoscyamus 3 m., dill water to  $\frac{1}{2}$  oz.

**Mist. Pot. Brom. (N.I.F.).** Potassium bromide 10 gr., liquid extract of liquorice 5 m., ammonium carbonate 1 gr., chloroform water to  $\frac{1}{2}$  oz.

**[P1] Mist. Pot. Brom. et Strych. (N.I.F.).**

Potassium bromide 10 gr., solution of strychnine hydrochloride 3 m., solution of bordeaux B 2 $\frac{1}{2}$  m., chloroform water to  $\frac{1}{2}$  oz.

**[P1] Mistura Bromidi et Digitalis (St. M. H.).**

Potassium bromide 20 gr., tincture of digitalis 5 m., potassium citrate 15 gr., compound tincture of cardamom  $\frac{1}{2}$  dr., peppermint water to 1 oz.

**[P1] Mist. Bromidorum (N.I.F.).**

Borax 5 gr., potassium bromide 5 gr., sodium bromide 5 gr., ammonium bromide 5 gr., arsenical solution 1 m., liquid extract of liquorice 5 m., chloroform water to  $\frac{1}{2}$  oz.

**[P1] Mistura Dysmenorrhœica (E.G.A.).**

Potassium bromide 15 gr., sal volatile, tincture of hyoscyamus a.a.  $\frac{1}{2}$  dr., spirit of chloroform 10 m., water to  $\frac{1}{2}$  oz.

**Tabellæ Potassii Bromidi (B.P.C.)** contain 5 gr. (0.3 g.).

**Cerebrom (C. F. Thackeray, Leeds).** A flavoured bromide preparation. Each fluid drachm contains potassium and sodium bromide 5 gr., ammonium bromide 3 gr., calcium bromide 1 $\frac{1}{2}$  gr., lithium bromide  $\frac{1}{2}$  gr. *Dose.*—1 to 2 fluid drachms diluted.

**Sedin (Hommel's Hæmatogen Co., London).** Tablets contain potassium bromide and sodium bromide of each 0.4 g., ammonium bromide 0.2 g., sodium chloride 0.1 g., with vegetable extractive. To make a sedative bouillon.

**[P1-S1] Gelineau Dragées (Mousnier-Delorme, Antony (Seine); Wilcox, Jozéau, London).** Dragées contain potassium bromide 1.0 g., antimony arsenate 0.001 g., picrotoxin 0.0005 g. *Dose.*—1st week, 1 twice daily; 2nd and 3rd weeks, 1 thrice daily; 4th week, 1 four times daily, and this dose (or larger if necessary) continued for 6 months or longer. For epilepsy.

**Sodii Bromidum (B.P., U.S.P., XI, Fr. Cx.).** NaBr=102.9.

*Dose.*—5 to 30 grains (0.3 to 2 g.). U.S.P. XI average dose 15 grains.

**(Natrium Bromatum (P.G., P. Helv. V, P. Jap. V, P. Hung.)** is sodium bromide. Sodium bromate, NaBrO<sub>3</sub>, is called **Natrium Bromicum** in Germany.)

In white deliquescent granular crystals, with saline taste.

**Soluble** 1 in 1½ of water, 1 in 16 of alcohol 90%.

**Uses.** In insomnia, maniacal attacks and hysteria. Full doses combat morphine habit, and may be given as a sedative in alcoholism. A 1% solution has been given by subdural injection, after removal of 50 to 60 ml. of cerebrospinal fluid, for delirium tremens.

It is used in the treatment of epilepsy in a similar manner to potassium bromide. Alternatively it may be used as a substitute for salt in the so-called "saltless" treatment of epilepsy, on the theory that diminishing the chloride increases the readiness with which bromide enters the blood stream (*see also* p. 65).

10 ml. of 10% solution intravenously has been recommended in eczema. 2 to 5 injections usually sufficient but more are sometimes needed.

The addition of 20 drops of sal volatile, or 5 drops of Fowler's Solution to each dose prevents the rash which often disfigures patients taking bromide.

**EPILEPSY.** The following is a typical hospital mixture for treatment of epilepsy: sodium bromide 5 to 15 gr., borax 5 to 10 gr., tincture of belladonna 5 to 10 m., liquor arsenicalis 1 to 3 m., chloroform water to ½ oz. *Dose.*—½ ounce thrice daily after meals.—D. Brinton, *Practitioner*, i/1936, 521.

Final remissions beginning with the institution of treatment or shortly after occurred in 35 of 96 cases (36%). Final remissions of over a year were brought about in 45.8% of 85 cases treated over a year. Remissions of over one year were brought about in 71.7% of 85 cases treated over one year—in some the remission lasted over ten years. In patients suffering from grand mal attacks only, the attacks were stopped in 43%. Of all cases those presenting focal attacks were most resistant to treatment, it being ineffectual in 55.3%. When remissions are brought about by treatment it must be continued throughout the life of the patient. It is suggested that early treatment and few previous attacks lead to more prompt and continued remissions.—L. J. Pollock, *J. Amer. med. Ass.*, i/1938, 632.

**HYPERCHLORHYDRIA.** Sodium bromide, 2 to 3 g. a day. Harmless in doses of 6 to 7 g. even when continued for some time.—*Brit. med. J. Epit.*, i/1936, 60.

**TRIGEMINAL NEURALGIA.** Many patients find considerable temporary relief, at least in the earliest stages, from the following mixture: sodium bromide 10 gr., tincture of gelsemium 10 m., butylchloral hydrate 5 gr., peppermint water to ½ oz. *Dose.*—½ ounce thrice daily, after meals.—D. Brinton, *Practitioner*, i/1936, 526.

**Sebrex** (*Allen & Hanburys, London*). Sedative broth tablets containing 17 grains of sodium bromide.

**Sedobrol Tablets** (*Roche Products, Welwyn Garden City*). Contain 17 gr. of sodium bromide in vegetable extractives and fat. Suggested for salt-free bromide treatment or diet—the tablet being simply covered with 100 to 200 ml. of hot water to produce a bouillon for use in nervous affections, epilepsy and migraine.

*Dose.*—1 to 6 tablets *per diem*.

**Strontii Bromidum** (*B.P.C., Fr. Cx.*).  $\text{SrBr}_2 \cdot 6\text{H}_2\text{O} = 355.6$ .

*Dose.*—5 to 30 grains (0.3 to 2 g.).

In deliquescent crystals, with bitter saline taste, **soluble** 2 in 1 of water, 1 in 3 of alcohol.

**Used** in gastric affections, dyspepsia, and vomiting of nervous origin; also in epilepsy instead of the potassium salt, but is more slowly absorbed.

# ACIDUM HYDROCHLORICUM

(with METALLIC CHLORIDES)

HCl = 36.46.

[P2] "*Hydrochloric acid.*"

[83] "*Hydrochloric acid—in substances containing less than 9%, weight in weight, of hydrochloric acid (HCl).*"

B.P. has sp. gr. 1.158 to 1.168, containing 32% *w/w* of HCl. P. Ned. V and P. Helv. V 25%. Fr. Cx. 35.5%. F.E. VIII 33.65%. P.G. VI 24.8 to 25.2%. P. Ital. V 35.39%. P. Belg. IV 36.47%. U.S.P. XI 35 to 37%. P. Jap. V 30%.

**Incompatible** with alkalis, alkaline carbonates, metallic oxides, silver, mercury and lead salts.

**Antidotes.** Treat as for poisoning by glacial acetic acid, see p. 7.

**Uses.** Escharotic, but less corrosive than sulphuric or nitric acid. Neuritis is sometimes treated by applying strong hydrochloric acid to the skin along the line of the inflamed and painful nerve on a wad of cotton wool; results are striking and appreciated. The freshly diluted acid, 5 to 10 m. with 6 to 8 oz. of water (Bouchard's remedy), taken with every meal, is of value in alimentary toxæmia.

## Acidum Hydrochloricum Dilutum (B.P.).

**Dose.**—5 to 60 minims (0.3 to 4 ml.).

Is prepared by diluting 31.3 g. of the strong acid with water to 100 g. An acid of approximately the same strength is obtained by diluting 5 fl. oz. 310 m. of the strong acid with water to 1 pint. Sp. gr. 1.045 to 1.052. Contains (B.P., U.S.P. XI, Fr. Cx., P. Jap. V, P. Helv. V, F.E. VIII and F. Norsk.) 10% *w/w* of HCl. P. Ital. V 8.07%, P. Ned. V is 4N (14.5%), P.G. VI 12.4 to 12.6%, P. Belg. IV 7.29%, P. Dan. 7.05%.

**Uses.** In conditions of achlorhydria (*e.g.*, in pernicious anæmia, chronic gastritis, cancer of the stomach, etc.) and hypochlorhydria (*e.g.*, in sprue).  $\frac{1}{2}$  to 1 dr. with meals has been recommended for tuberculous diarrhœa. In dilatation of the stomach 10 to 15 minims after each meal may be given with or without 6 to 8 grains of pepsin.

**PRURITUS VULVÆ.** A common factor present in pruritus vulvæ, leukoplakia, kraurosis vulvæ and leukoplakic vulvitis is achlorhydria, which causes a deficiency of absorption of vitamin A from the diet. The addition of diluted hydrochloric acid to the diet of 42 women suffering from intractable pruritus vulvæ with achlorhydria relieved the pruritus in the majority of cases, with great improvement of the local vulval condition. The diluted hydrochloric acid is given by mouth, a teaspoonful in a glass of water. Half of this solution is sipped during the meal and the other half drunk after the meal. The acid is taken with each meal and continued for several weeks. A teaspoonful of cod-liver oil is also taken three times a day.—B. H. Swift, per *J. Amer. med. Ass.*, 1/1937, 1754.

## Betainæ Hydrochloridum. $C_5H_{11}NO_2 \cdot HCl = 153.6$ .

(Betaine (*Syn.* TRIMETHYL-GLYCOCOLL.  $C_5H_{11}NO_2 = 117.1$ ) occurs in beets and mangolds (especially *unripe* roots) and has been found in a number of vegetable and animal substances. It

is formed on oxidation of choline and is chemically related to muscarine and neurine.)

*Dose.*—1 to 8 grains (0.06 to 0.5 g.).

White crystalline substance soluble in water 1 in 2; in alcohol about 1 in 20.

*Uses.* Liberates hydrochloric acid (almost 25% of its weight), and is given with pepsin or diluted with water in gastric affections.

*Acidol* (*Bayer Products, London*). Betaine hydrochloride in  $7\frac{1}{2}$  gr. tablets.

*Acidol-Pepsin* (*Bayer Products, London*).

*Dose.*—1 to 2 tablets ( $7\frac{1}{2}$  grains in each) in water after meals.

Contains betaine hydrochloride equivalent to 8 m. of dilute hydrochloric acid, and pepsin  $1\frac{1}{2}$  gr. In anorexia, hypochlorhydria, gastritis, etc.

*Acidulin* (*Eli Lilly, London*). Glutamic acid hydrochloride. Liberates free HCl in presence of moisture. Capsules contain the equivalent of 10 drops of dilute HCl. For use in the treatment of conditions exhibiting deficiency of gastric HCl.

*Betacid* (*Richter, London*). Betaine hydrochloride and pepsin. Available in two strengths:—"Mite" containing betaine hydrochloride  $\frac{1}{2}$  gr., pepsin  $3\frac{1}{2}$  gr. and "Forte" containing betaine hydrochloride  $6\frac{1}{2}$  gr., pepsin  $1\frac{1}{2}$  gr.

*Paractol* (*Camden Chemical Co., London*). Betaine hydrochloride and glutamine hydrochloride in powder form for the treatment of gastric disturbances due to insufficiency of HCl. 3 g. is equivalent to 37 drops of dilute hydrochloric acid. *Dose.*—45 grains (3 g.) in water.

**Ammonii Chloridum** (*B.P., U.S.P. XI, Fr. Cx., P. Helv. V*).  $\text{NH}_4\text{Cl} = 53.50$ .

*Dose.*—5 to 60 grains (0.3 to 4 g.).

White crystals soluble 1 in 3 of water, 1 in 60 alcohol (90%), and 1 in 5 of glycerin.

*Incompatible* with alkalis and carbonates of alkaline earths.

*Uses.* Mildly expectorant, diaphoretic and diuretic. Is administered to render the urine acid in the treatment of urinary infections, e.g., with mandelic acid; change of pH alone has no effect on bacilluria.

In cases of chronic lead poisoning, ammonium chloride, in a dose of 1 or 2 g. daily in divided doses, produces a condition of acidosis which hastens the elimination of the lead; too rapid elimination should be avoided, however.

**URINARY AFFECTIONS.** In cases of infection with the proteus bacillus, ammonium chloride would seem to be unsuitable as a urinary acidifier for biochemical and bacteriological reasons. In treating infections of the kidneys with the proteus bacillus, systemic acidification may be dangerous and lead to the formation of new stones, unless one is successful in obtaining a strongly acid urine. This may be due to the rapid manufacture of ammonia by the proteus bacilli.—R. Chute, *New Engl. J. Med.*, i/1936, 869. See also D. M. Lyon and D. M. Dunlop, *Brit. med. J.*, ii/1935, 1096.

**Collyrium Ammonii Chloridi** (*B.P.C.*). 0.5% w/v.

*Lot. Evap. Meth.* (*N.I.F.*).

Industrial methylated spirit 1 oz., ammonium chloride 2 dr., water to 8 oz.

**Mist. Ammon. Chlorid.** (*N.I.F.*). Ammonium chloride 15 gr., aromatic solution of ammonia 5 m., liquid extract of liquorice 15 m., water to  $\frac{1}{2}$  oz.

[P1] **Mist. Ammon. Chlorid. Co.** (*N.I.F.*)

Ammonium carbonate 3 gr., ammonium chloride 5 gr., tincture of chloroform and morphine 5 m., liquid extract of liquorice 5 m., water to  $\frac{1}{2}$  oz.

**Pastilli Ammonii Chloridi** (*B.P.C.*) contain 2 gr. (0.13 g.).

**Pastilli Ammonii Chloridi Compositi** (*B.P.C.*) contain 2 gr. of ammonium chloride and 2 m. of liquid extract of liquorice.

**Trochisci Ammonii Chloridi Compositi (B.P.C.)** *Syn.* TROCHISCI AMMONII CHLORIDI ET GLYCYRRHIZÆ.

Contain 3 gr. of ammonium chloride and 3 gr. of extract of liquorice. Tablets are also made same strength.

**Trochisci Ammonii Chloridi (T.H.).** 2 grains, marked "M.A." One every 3 hours useful in congestion of the pharynx and larynx, loss of voice arising from cold and bronchial cough.

**Trochisci Ammonii Chloridi Compositi (T.H.).** Contain ammonium chloride 1 gr., potassium chlorate 2 gr., and  $\frac{1}{2}$  gr. approximately of cubeb. Marked "C.M.A."

**Calcii Chloridum (B.P., F.E. VIII).**  $\text{CaCl}_2 = 111.0$ .

*Dose.*—*Per os*, 10 to 30 grains (0.6 to 2 g.). *B.P. Add. I* states that when calcium chloride is prescribed for injection hydrated calcium chloride shall be dispensed.

This is the anhydrous salt, the *B.P.* requiring not more than 10% of water. In fused white agglutinated very deliquescent masses.

**Soluble** 1 in  $\frac{1}{2}$  of water, 1 in 3 of alcohol 90%.

**Calcii Chloridum Hydratum (B.P. Add. I, Fr. Cx., P. Helv. V, P. Belg. IV, P. Ital. V, P. Jap. V).**  $\text{CaCl}_2 \cdot 6\text{H}_2\text{O} = 219.1$ .

*Dose.*—By intramuscular injection, 1 to 3 grains (0.06 to 0.2 g.); by intravenous injection, 10 to 30 grains (0.6 to 2 g.). It should never be given hypodermically, owing to its destructive action on the subcutaneous tissues, and intravenously it should be employed with caution owing to possible formation of blood clot.

In colourless deliquescent crystals with slightly bitter taste, containing about 50% of  $\text{CaCl}_2$ .

**Soluble** 4 in 1 of water, 1 in 1 of alcohol 90%.

**Incompatible** with carbonates, phosphates, sulphates and tartrates.

**Uses.** Calcium chloride increases the coagulability of the blood and has thus been employed in a wide variety of hæmorrhagic conditions, though there is little convincing evidence of its value.

It is employed in itching skin affections, *e.g.*, pruritus, prurigo, urticaria. It is useful in chilblains (full dose frequently), in certain forms of headache, in tubercular disease, chorea, glandular affections and in all conditions in which there is calcium deficiency.

The use of calcium chloride should be restricted to those conditions in which it is desired (1) to raise the serum calcium and more especially to increase the proportion of ionised calcium, and (2) to increase the acidity (pH) of the urine. It may be given in doses of 15 to 30 grains four-hourly, but prolonged administration is inadvisable in view of the possibility of acidosis. Given by injection it is irritating and its use should be avoided if possible, even for intravenous injections, since a small amount leaking into the perivascular tissues may cause considerable pain and sloughing. Subcutaneous injections of calcium preparations are of little value, since a reasonable amount cannot be given by this route.—N. Morris, *Practitioner*, ii/1939, 343.

**ACNE.** A 10% solution of calcium chloride intravenously, 5 ml. every third day, increased to 10 ml. every second day, of value. Inject slowly, taking care not to infiltrate the skin or the hypoderm. When patient complains of heat in the face, stop till this feeling disappears.—*Per Prescriber*, 1929, 332.

**ANGIONEUROTIC ŒDEMA** treated with 10 grain doses thrice daily, increasing to 20 grains. The swellings which appeared continuously in different parts of the body disappeared completely.

**CANCER OF THE BUCCAL CAVITY.** For the prevention of pneumonia after operations on the tongue and mouth for cancer. For about a week before operation give 15 gr. calcium chloride thrice daily (practically all cases of cancer are deficient in calcium).—James Barr, *Brit. med. J.*, i/1934, 452.

**CHOREA.** There is a rather low total serum calcium content. The calcium content of the cerebrospinal fluid is consistently low.—E. C. Warner, *Lancet*, i/1930, 339.

**ECLAMPSIA.** Calcium therapy is the prophylactic. Continuous administration during pregnancy of 15 gr. calcium phosphate in  $\frac{1}{2}$  oz. of water thrice daily as prophylactic in midwifery, combined with a 1 in 1000 solution of acriflavine in glycerin (*q.v.*) for vaginal injection.—J. L. Moir, *Brit. med. J.*, i/1931, 118.

Calcium therapy in eclampsia disappointing. The fits are not influenced by the calcium content of the serum.—W. C. W. Nixon, *Lancet*, ii/1931, 292.

**EPIDIDYMITIS** well treated by intravenous injection of 0.5 to 1 g. in dilute solution—4 or 5 injections, one daily.—Per *J. Amer. med. Ass.*, ii/1928, 1136.

**HÆMORRHAGE** (uterine) may be controlled by intramuscular injection of calcium chloride. 1 gr. in 100 m. injected *deeply* into the gluteal muscles is generally painless. A second injection at end of 24 hours and a third, 24 hours later, may be given.

**HAY FEVER.** A low body content of calcium is favourable to hay fever, the administration of calcium chloride acting beneficially. A retention of potassium and a greater output of sodium results from increased calcium in the diet. 10 grain doses *t.d.* have been advised.

**NEPHRITIS and EDEMA** successfully treated with calcium chloride,  $2\frac{1}{2}$  to  $4\frac{1}{2}$  dr. daily, free diuresis occurring.

In chronic parenchymatous nephritis the calcium is at a low level.—Dan T. Davies, *Lancet*, i/1930, 203.

**TETANY.** Intravenous injection of 10 ml. of a 10% solution of calcium chloride is an excellent emergency measure for the relief of symptoms of parathyroid tetany. A good method of treatment is to give orally a large amount of calcium chloride (150 grains daily); where this is not effective, and where achlorhydria is present, give 50 to 100 ml. of N/3 hydrochloric acid in milk (1 of acid to 20 of milk) to increase absorption of the calcium.—D. Campbell, *Lancet*, i/1935, 372.

In acute cases of spasmodophilia the calcium content of the serum ranges between 4 and 8 mg. per 100 ml. Give calcium chloride 2 g. every 2 hours. As much as 6 g. can be given in 24 hours in milk to an infant without any apparent intolerance. Improvement in  $\frac{1}{2}$  hour. Hydrochloric acid (*e.g.*, 260 ml. of N/10 acid with 750 ml. of milk) and ammonium chloride, 5 g. a day, also efficacious but they are only transient in effect.—Dan T. Davies, *Lancet*, i/1930, 202.

#### **Mistura Calcii Chloridi (N.I.F.).**

Calcium chloride 10 gr., syrup of ginger  $\frac{1}{2}$  dr., water to  $\frac{1}{2}$  ounce.

**Mist. Calc. Chlorid. c. Ferro (N.I.F.).** Calcium chloride 10 gr., solution of ferric chloride 10 m., water to  $\frac{1}{2}$  oz.

#### **Mistura Calcii Chloridi Albuminata (B.V.H.).**

Calcium chloride 15 gr., solution of pectin 2 dr., syrup 30 m., water to 1 oz. (Solution of pectin contains pectin (100 grade) 87.5 gr., glycerin of chlorbutol (1 in 12)  $\frac{1}{2}$  oz., water to 20 oz.).

A calcium mixture for oral administration over long periods to asthmatic and arthritic patients; it does not cause derangement of the stomach.—*Pharm. J.*, ii/1934, 620.

### **Syrupus Calcii Chloridi (B.P.C.). Syn. ELIXIR CALCII CHLORIDI.**

**Dose.**—1 to 2 drachms (2 to 4 ml.).

Calcium chloride 1 in 8 in distilled water and syrup of lemon.

**Transcutan (Transcutan Ltd., Leeds).** A concentrated solution of mineral salts from the Kreuznach springs, containing calcium chloride, iodine, bromine, strontium and lithium salts, with aromatic oils, for adding to baths. In rheumatoid arthritis, fibrositis, etc.

**Magnesii Chloridum** (*B.P.C., Fr. Cx., P. Helv. V.*).  
 $\text{MgCl}_2 \cdot 6\text{H}_2\text{O} = 203.3$ .

*Dose.*— $\frac{1}{4}$  to 1 ounce (8 to 30 g.).

Deliquescent crystals, **soluble** about 2 in 1 of water and 1 in 6 of alcohol 90%. Mild purgative, a dose in  $\frac{1}{2}$  pint of hot water useful for constipation and in dyspepsia and stomach disorders.

**Potassii Chloridum** (*B.P.C., P. Helv. V, P. Dan.*).  
 $\text{KCl} = 74.55$ .

*Dose.*—15 to 60 grains (1 to 4 g.). A 25% aqueous solution is usually better tolerated than capsules or tablets; a teaspoonful of this solution (equivalent to 1 g. of the salt) added to a wineglassful of water or milk seldom gives rise to gastric distress. It is well to test the patient's tolerance with an initial dose of 15 gr.

**(Kalium Chloratum** (*P. Jap. V, P. Helv. V*) is potassium chloride. Potassium chlorate (*P. Jap. V, P. Helv. V, P. G. VI*) is **Kalium Chloricum**.)

Potassium chloride is obtained from natural sources or by neutralising hydrochloric acid by potassium carbonate, and occurs as a colourless, crystalline solid, with a saline taste.

**Soluble** 1 in 3 of water; insoluble in alcohol and ether.

**Uses.** Potassium chloride has been advocated for use in place of table salt in gouty and rheumatic individuals as a means of preventing the formation of uric acid calculi. It has also been found of value as a diuretic in the treatment of nephritis with oedema, the main objection to its use in this connection being that if its elimination is delayed it may give rise to toxic symptoms, such as chilliness, fatigue and headache.

In common with most of the potassium salts the toxicity of potassium chloride by the mouth in healthy individuals is very slight, and the ill effects arising from the ingestion of excessive amounts are few, since gastric upset usually occurs before a toxic amount has been taken, and this retards assimilation. In the presence of renal insufficiency, however, even the amount of potassium contained in an ordinary diet may be dangerous, and potassium salts should only be administered with caution. Their use should also be avoided in the presence of cardiovascular disease, owing to their depressant effect on the heart, and they should be employed with care when given simultaneously with digitalis, since the two drugs may act synergically on the heart.

Although in the treatment of Addison's disease a low potassium intake is recommended in order to favour the retention of sodium, over-treatment, when due to excessive administration of desoxycorticosterone acetate (*q.v.*), may result in a decrease in the concentration of serum potassium resulting in an exacerbation of certain of the symptoms, and to the occurrence of oedema and hypertension, and in this case an increased potassium intake is advised.

During recent years a considerable amount of work has been done on the biochemistry of potassium salts and the indications



for their use (and in particular for the use of potassium chloride) are now more precise and less empirical. In the light of present knowledge it would appear that the action of potassium depends on its effects (1) as an electrolyte, (2) as a substance concerned with carbohydrate metabolism, (3) as a mediator of the nerve impulse, and (4) as a participant in muscle contraction. On the basis of this knowledge potassium salts have been employed with varying success in a wide variety of conditions, *e.g.*, in hay fever and other allergic diseases, in familial periodic paralysis, in myasthenia gravis, and in Ménière's disease.

**ADDISON'S DISEASE.** The potassium content of the diet of patients with Addison's disease affects the course of the disease and the development of the symptoms of crisis. An intake of potassium not greater than 4 g. a day, an amount comparable to that contained in a normal diet, may promote the excretion of sodium and chloride whereby significant losses of sodium and chloride occur and symptoms of crisis are precipitated. If the intake of potassium is restricted to about 1.6 g. per day, the requirement of sodium and chloride is materially diminished and it becomes possible (though not necessarily desirable) to maintain patients with smaller doses of sodium salts than are otherwise needed and without injections of extract of adrenal cortex. Optimal therapeutic results demand not only restriction of potassium but optimal rather than minimal doses of sodium salts, and when possible injection of an active extract of adrenal cortex. The arrangement of a diet to contain not more than 1.6 g. of potassium requires careful planning, and the diet should be suitably supplemented by the addition of calcium phosphate, some iron salt, and a concentrate of vitamins B and G.—R. M. Wilder *et al.*, *Arch. intern. Med.*, 1937, 59, 367.

Directions for the planning and preparation of diets low in content of potassium, including tables showing the potassium content of a wide variety of fruits, vegetables, and other foods.—M. Victor, *Proc. Mayo Clin.*, 1937, 424.

**FAMILIAL PERIODIC PARALYSIS.** Administration of potassium caused rapid disappearance of paralysis. Potassium chloride, from 5 to 10 g. in watery solution by mouth, brought about return of movement within thirty minutes to one hour and the ability to walk unaided within two hours. Recovery was associated with a progressive rise of serum potassium. Intravenous injections (50 ml. of 2% solution in 10 minutes) caused much more rapid and dramatic recovery but with intense burning pain.—R. H. Pudenz, *J. Amer. med. Ass.*, ii/1938, 2254.

It is well known that periodical attacks of paralysis are always accompanied by a fall in the potassium figure, and the administration of 5 to 10 g. by the mouth restores the power of movement within half to one hour. Complete cures have been reported in 8 to 10 days of infantile paralysis. Treatment should be started as early as possible, the daily dose for an adult being 5 to 6 g. and for an infant 0.75 to 1 g., the drug being given in 250 g. of syrup for an adult and 125 g. for an infant.—A. Ravina, *Pr. méd.*, 1939, 789.

**HÆMORRHAGE.** Dental hæmorrhage may be rapidly suppressed by insertion in the socket of a cotton plug soaked in 5% solution of potassium chloride. No irritation results.—J. A. Higgins, *J. Amer. dent. Ass.*, 1937, June, 1047.

**HAY FEVER.** Striking benefit was obtained from the use of potassium salts in 29 cases of hay fever. Most of the patients responded quickly to 5 grains (a dose of 10 grains caused acute epigastric pain) of potassium chloride, dissolved in water, three times a day, some experiencing relief in a few minutes and some in about half an hour. The treatment was also found of value in urticaria, eczema and other allergic diseases. It is suggested that allergy is predominantly a disturbance of electrolyte metabolism and associated with some endocrine (possibly adrenal) dysfunction.—B. Bloom, *J. Amer. med. Ass.*, ii/1938, 2281. Results not confirmed in 40 cases.—G. F. Harsh and P. B. Donovan, *ibid.*, i/1940, 1859; or in 153 cases.—S. S. Rubin *et al.*, *ibid.*, i/1940, 2359.

**MÉNIÈRE'S SYNDROME.** In forty patients treated by a high potassium intake with an otherwise normal diet, the therapeutic results were encouraging. It cannot be considered a cure for all the symptoms, but clinical improvement has been impressive, and surgical treatment was not carried out in any of the cases. A daily dose of 6 to 10 g. of potassium chloride in aqueous solution was given

and no dietary modifications were advised.—J. H. Talbott and M. R. Brown, *J. Amer. med. Ass.*, i/1940, 125.

**MYASTHENIA GRAVIS.** Potassium chloride given in large doses, 10 to 12 g., by the mouth, gives a demonstrable improvement in myasthenia. Six patients have taken the salt daily for two months in doses of from 4 to 6 g. six times a day—the largest total in one day being 40 g., and this treatment has proved a valuable adjunct to Prostigmin (*q.v.*). The only unpleasant symptom has been a mild diarrhoea and some nausea following the larger doses.—L. P. E. Laurent and W. W. Walther, *Lancet*, i/1935, 1434.

**OBESITY.** The use of potassium salts in the treatment of obesity has been recommended, a high protein intake supplemented by 4 g. or more of potassium chloride daily constituting an effective anti-obesity regimen.—Per *New Engl. J. Med.*, i/1940, 587.

**Sodii Chloridum** (*B.P., U.S.P. XI, Fr. Cx.*). NaCl = 58.45.

*Dose.*—10 to 60 grains (0.6 to 4 g.). White cubical crystals.

(**Natrium Chloratum** (*P.G. VI, P. Helv. V, P. Jap. V.*) is sodium chloride. Sodium chlorate, NaClO<sub>3</sub>, is called **Natrium Chloricum** in Germany.)

**Soluble** 1 in about 3 of water (not more in boiling water), about 1 in 200 of alcohol 90%, about 1 in 10 of glycerin.

**Uses.** Although in common use, sodium chloride is not requisite to those having ordinary mixed diet, but is necessary to vegetarians. Insufficient sodium chloride leads to anæmia, debility and œdema of face and ankles. Large doses are emetic.

As a purgative it may be given in dose of 120 to 240 grains. As a laxative, 75 grains in a tumbler of cold water, it is stated, acts efficiently and without pain. Rectal injections are used to kill threadworms. Hypodermically or intravenously as normal saline solution, *q.v.*

In large doses, 10 to 15 g. daily, sodium chloride is frequently of considerable value in the treatment of Addison's disease and may substantially reduce the dose of suprarenal cortex extract required. In some cases its administration may replace treatment with cortical extract, especially if the potassium intake is kept low (*cf.* Potassium Chloride).

**ADDISON'S DISEASE.** Striking results in a case from a dosage of 15 g. a day. The sodium in the blood is reduced in cases of Addison's disease.—G. Graham, *Lancet*, ii/1933, 1446.

Dramatic effect in a case put on 10 g. daily (in milk), relapse following reduction of dose to 5 g. daily. Treatment with sodium chloride is not in any way curative, but by supplying an excess of sodium makes good the wastage.—C. M. H. Howell, *Lancet*, i/1934, 1116. See also R. F. Loeb, *Proc. Soc. exp. Biol. Med.*, N.Y., 1933, 30, 808; W. G. Sears, *Lancet*, i/1934, 950.

Sodium chloride by mouth may be of real value in the acute, subacute and chronic phases of Addison's disease. On the other hand the benefit may be so slight as not to be appreciated by the patient. The emetic action of sodium chloride may prevent its administration by the mouth. Sometimes salts of sodium other than the chloride may be satisfactorily substituted to overcome the difficulty. 10 g. of the salt daily is as much as most patients can possibly take, but sometimes 20 g. or more is necessary.—S. L. Simpson, *Proc. R. Soc. Med.*, 1936, 29, 1143.

Most patients object to taking more than 10 g. of sodium chloride in the day except for a short while, and this will only supply 4 g. of sodium. It may be that some mixture of salts which will supply about 10 g. of sodium, will give better results. A trial should be made of a mixture of sodium chloride, sodium bicarbonate and sodium citrate, but a careful watch should be kept on the patient's alkali reserve.—G. Graham, *Proc. R. Soc. Med.*, 1936, 29, 1138.

**DIABETIC PAIN.** Complete or marked relief of neuritic pain in all of 13 diabetic patients following oral administration of sodium chloride in amounts ranging from 15 to 90 g. daily over periods of two to four weeks with interruptions of 10 to 14 days. The relief is thought to be due to a vasodilating effect, since observations indicate that ischaemia, the result of vascular disease, primarily arteriosclerosis, is responsible for the neuritic symptoms.—H. R. Sandstead and A. J. Beams, *Arch. intern. Med.*, 1938, 61, 372.

#### **Dechlorination or Salt-free Diet.**

**NEPHRITIS** has been treated by this (in many forms of nephritis the kidneys fail to eliminate salt). Copious diuresis sets in, cedema disappears and remains more or less absent so long as the treatment is kept up. Food should be cooked without it. The salt-free diet is, however, often disappointing. It should be tried where heart and lungs are hampered by excessive cedema, and in migraine and chlorosis. It is important to remember that it is the sodium ion that is important, and not the chlorine; thus, sodium bromide and sodium bicarbonate should also be avoided in these cases.

**EPILEPSY** has been treated by sodium chloride reduction. Reduce the salt in the diet and the absorption of bromide will increase. The combined treatment, e.g., with bromide tablets containing 2 gr. of salt and 18 gr. of bromide to be used to salt broth, is satisfactory.

**MÉNÈRE'S SYNDROME.** Severe attacks of vertigo and vomiting in 12 patients suffering from deafness and tinnitus ceased on the institution of a low sodium diet (water intake unrestricted) and administration of ammonium chloride 3 g. (in capsules) with each meal, the medication being given three days on and two days off. The addition of ammonium chloride prevents the storage of sodium. All medicaments containing sodium should be avoided, e.g., sodium salicylate, sodium bicarbonate, sodium bromide, etc.—M. R. Brown, *J. Amer. med. Ass.*, i/1937, 1158.

**Selarom** (*Bayer Products, London*). Mixture of calcium, magnesium, and sodium salts of organic acids. For salt-free dietary.

**Balneum Sodii Chloridi** (*B.P.C.*). Contains 7 lbs. of sodium chloride per 30 gallons. A tonic and stimulant, e.g., in chronic rheumatism.

#### **Collunarium Plasma** (*B.V.H.*).

Sodium chloride 6 dr., sodium sulphate 2 dr., sodium phosphate 2 dr., sucrose 3 oz. (Apoth.) or tragacanth 20 gr., thymol 3 gr., menthol 3 gr., alcohol 90% 1 dr., distilled water to 6 oz.

#### **Hauftus Sodii Chloridi Compositus** (*Mid. H.*).

Sodium chloride 5 gr., sodium bicarbonate 5 gr., spirit of chloroform 5 m., caraway water to 1 oz. For the dry cough of the early stages of acute bronchitis.

**Liquor Sodii Chloridi Physiologicus** (*B.P.*). *Syn.* **PHYSIOLOGICAL SALINE SOLUTION, NORMAL SALINE SOLUTION.**

A sterile 0.9% w/v aqueous solution of sodium chloride. *U.S.P. XI* and *P. Jap. V* have 0.85%, and *Fr. Cx.* 0.8%.

This is isotonic with the liquid of the blood corpuscles and possesses the same osmotic pressure as the *liquor sanguinis*; it has a freezing point of approximately  $-0.56^{\circ}$ . The injection should be made at least at  $105^{\circ}\text{F}$ . (*this is important*), into any convenient vein. The rate of injection varies; it may be as rapid as a pint in 10 minutes, or as slow as 8 ounces per hour (see refs. *infra*).

Fortunately only an approximation to an isotonic solution is necessary, as mucous membranes are practically insusceptible to changes in osmotic pressure within fairly wide limits. The solution should be slightly alkalisied. 0.1% sodium bicarbonate is sufficient.

**ISOTONIC SODIUM CHLORIDE** for ophthalmic use is 1.4%. The lachrymal secretion is stated to contain 1.3% of sodium chloride and 0.5% of albumin. Eye lotions are often made isotonic.

**Uses.** Normal saline solution, usually given by intravenous or rectal injection, is an easy and effective means of increasing the

blood volume and blood pressure, and is of great value in severe hæmorrhage, surgical shock, acute diarrhœa, and the recurrent vomiting of infants. By hastening excretion of poisons by the kidneys, intravenous injections are also of value in morphine poisoning, uræmia, and diabetic coma.

**Continuous intravenous saline** preferable to putting into the circulation a pint or more of fluid comparatively suddenly. The cannula (preferably gold-plated) is tied into a vein a little larger than itself, either in the back of the hand or the saphena or one of its branches, just below the knee, or the vein just in front of the internal malleolus, the vein being exposed by a transverse incision after infiltration anæsthesia. The cannula and wound should be moist with citrate solution at time of introduction. A splint is used to keep the limb at rest. The fluids generally used are normal saline or 5% glucose in normal saline, kept warm by placing an electric heating pad on the limb over the cannula. The average rate of flow for an adult is 50 drops per minute ( $\frac{1}{2}$  pint an hour), increased to 100 drops in the first hour if necessary (œdema the signal for reducing flow). May be continued for 3 to 7 days.—V. Bailey and J. M. Carnow, *Brit. med. J.*, i/1934, 11. Value confirmed by E. R. Flint, *ibid.*, 75; W. Morris, *ibid.*, 75. In almost constant use at the Northampton General Hospital since June, 1931.—E. L. Laver, *ibid.*, 123.

**ACNE.** Intravenous injections of 100 ml. increased by 50 ml. until a maximum of 250 ml. was reached (unless the patient had only one or two pus pockets, when the solution was injected locally into the pus and around the inflammatory base); most serviceable in pustular acne and furunculosis.—H. Goodman, *Arch. Derm. Syph.*, June, 1935, 828.

**GONORRHEA.** 1% saline solution has many advantages over a 1 in 10,000 potassium permanganate solution for posterior irrigation.—*Brit. med. J. Epit.*, ii/1929, 43.

**ILEUS.** As in cholera, there is dehydration. Give  $2\frac{1}{2}$  to  $3\frac{1}{2}$  pints of normal saline intravenously.—D. C. Corry, *Brit. med. J.*, i/1931, 219.

**RETAINED PLACENTA.**—The rapid injection of 350 to 400 ml. of saline into the umbilical vein in cases of retained placenta is a successful and much less dangerous undertaking than the manual removal of this organ.—David Levi, *Practitioner*, i/1936, 508.

**SCIATICA.** Injection of normal saline into and around the sciatic sheath is of value in the later stages of trunk sciatica (sometimes known as low sciatica or true sciatica). On entering the nerve sheath, employing a lumbar puncture needle of 10 cm., inject 20 ml. of the solution very slowly and leave the needle in position; then refill the syringe. Having fixed the syringe in position, slightly withdraw the needle and push upwards into the piriformis muscle and inject a further 50 ml. It is a good plan to include 10 ml. of 1% Novocain in the normal saline mixtures made up to 100 ml. It is only in trunk sciatica that these injections are of any use.—J. B. Burt, *Practitioner*, ii/1939, 275.

**SURGICAL SHOCK.** Instead of saline injections, gum saline-Bayliss (sodium chloride 2 g., potassium chloride 0.05 g., calcium chloride 0.05 g., acacia 5 g., distilled water 100 ml.) is advocated for loss of blood if actual blood transfusion is impossible.—H. Pritchard, *Brit. med. J.*, i/1927, 793. (See *Acacia*.)

**Solvellæ Sodii Chloridi (B.P.C.)** contain 20 gr. (1.3 g.).

**Ringer's Solution (B.P.C.).** Sodium chloride 0.7, potassium chloride 0.014, calcium chloride 0.012, sodium bicarbonate 0.02, water to 100. Is isotonic with the serum of frog's blood.

The Committee on Pharmacy and Pharmacognosy of the Pharmacopœia Commission (*Report 13*) have recommended the inclusion in the *B.P.* of the following formula for Ringer's Solution:—sodium chloride 9 g., potassium chloride 0.42 g., hydrated calcium chloride 0.48 g., sodium bicarbonate 0.5 g., water to 1000 ml.

**Liquor Ringeri (P. Jap. V)** contains sodium chloride 0.8%, potassium chloride 0.075%, calcium chloride 0.02%, sodium bicarbonate 0.01%.

**Ringer-Locke Solution (B.P.C.).** Sodium chloride 0.9, potassium chloride 0.042, calcium chloride 0.024, dextrose 0.1, sodium bicarbonate 0.05, water to 100. Is isotonic with the serum of mammalian blood.

**Liquor Lockei (P. Jap. V)** contains sodium chloride 0.9%, potassium chloride 0.025%, calcium chloride 0.046%, dextrose 0.1%, and sodium bicarbonate 0.02%.

**AURICULAR FIBRILLATION.** There is always calcium deficiency. Ringer's solution containing about double the usual amount of calcium chloride and 2 ounces of syrup of glucose to the pint is a good drink which should be drunk freely.—Sir J. Barr, *Brit. med. J.*, i/1930, 774.

**Ringer-Tyrode Solution (B.P.C.).** Sodium chloride 0.8, potassium chloride 0.02, calcium chloride 0.02, magnesium chloride 0.001, dextrose 0.1, sodium acid phosphate 0.005, sodium bicarbonate 0.1, water to 100. Is isotonic with the serum of mammalian blood.

**Fischer's Modified Ringer's Solution.**

Sodium chloride 0.5, calcium chloride 0.04, potassium chloride 0.02, distilled water to 100. This is employed in surgical practice instead of normal saline, e.g., for dissolving procaine. Has advantages over Ringer's or Tyrode's solution. This solution possesses constant pH value of 7.52 at 37°, is isotonic with blood, is sterilisable and contains calcium and potassium in a ratio approximating to that in arterial blood. Similar relation exists between total uni- and bivalent positive ions.

**STOCK SOLUTION** contains sodium chloride 10.5 g., potassium chloride 0.5 g., magnesium chloride 0.1 g., calcium chloride 0.3 g., N/1 phosphoric acid 5 ml., and 50 ml. of water.

For use filter 50 ml. and add 1 litre of water, heat and when cool saturate with oxygen, and add 5 ml. of sterile N/1 sodium carbonate solution.

**Hypertonic Saline Solution.** Intravenous injections of hypertonic saline solutions, varying in strength from 5 to 30%, are of value in conditions in which it is desired to replace loss of body fluids and chlorides, e.g., in cholera (120 grains of sodium chloride and 4 grains of calcium chloride in a pint of distilled water). They also lower the pressure of the cerebrospinal fluid and give relief in post-concussional headache, cerebral tumour, and cerebral hernia. The injection in divided amounts of from 100 to 200 ml. of a 5 to 10% solution is of value after operation in acute intestinal obstruction. A 20% solution has been employed as a sclerosing agent for varicose veins, but is said to be more painful and less certain than quinine urethane.

40 ml. of a 30% saline solution intravenously is an effective means of raising the blood pressure immediately after the fall which follows the administration of a spinal anæsthetic—it also reduces the number of post-operative headaches.—H. Dodd, *Lancet*, i/1940, 360.

**ACUTE INTESTINAL OBSTRUCTION** well treated immediately after operation by 20 g. of sodium chloride intravenously in 10% solution 30 ml. at a time during 48 hours (maximum 70 g. for a man of average weight) with 1 litre physiological serum subcutaneously during the same period.—*Brit. med. J. Epit.*, i/1928, 32.

Discussion at B.M.A. Centen. Meeting, 1932, *Sir W. I. de C. Wheeler*.—Hypertonic saline intravenously reduced mortality rate from 50 to 11.1%. *D. P. D. Wilkie*.—Fluids and chlorides must be given liberally before operation. *R. Graham* (Toronto).—Thousands of ml. of saline necessary in these cases.—*Brit. med. J.*, ii/1932, 364.

**ANGINA PECTORIS** due to coronary artery disease. Injections used with good results in patients not improved by rest or the usual therapy. Initial dose 100 ml. of 5% sodium chloride solution, and subsequent doses increased by 50 ml. weekly up to a maximum of 250 ml., injections being given three times weekly. Contraindications are nephritis, cardiac decompensation and arterial hypertension of over 180 mm. of mercury. Injection discontinued if precordial pain occurs during or immediately following.—S. C. Feinberg, *Amer. J. med. Sci.*, 1936, 191, 210.

**CARBUNCLES.** The local application employed is a fomentation or compress of fluffed-up white gauze well wrung out of a hot solution of hypertonic salt—one ounce to the pint—renewed two-hourly during the day and four-hourly at night. In a few days the slough comes away entirely, when dry fluffed gauze dressings are substituted. The method is equally applicable to boils. In infections of the face, nose and lip the part is bathed in the hypertonic salt solution for a quarter of an hour at a time at two or three-hourly intervals, a compress being applied as near as possible during the intervals.—C. Donald, *Brit. med. J.*, i/1935, 963.

**POST-CONCUSSIONAL STATES.** One of the effects of injecting hypertonic saline into the circulation is a diminution in the volume of the brain—hence of use in post-concussional or post-concussional states—for relief of headache—even 100 ml. of 30% solution can be given, but usually 50 ml. of 15% effective.—A. Feiling, *Brit. med. J.*, ii/1930, 907.

**TRICHOMONAS VAGINITIS.** Vaginal douching with 25% salt solution gives prompt relief and in most cases prevents recurrence. The effect is due to osmotic action, and is non-irritating and inexpensive.—L. Rosenthal and co-workers, *J. Amer. med. Ass.*, ii/1935, 105.

**VARICOSE VEINS.** Large amounts may be injected, 10 ml. for one injection, up to 20 or 30 ml. at one time; or with 5 or 10 ml., 3 or 4 injections at one sitting. A more adherent and exclusive thrombosis and a better end-result than with other agents.

Sodium chloride 20% the "safest as far as systemic reaction is concerned." Retards clotting of the blood, and incapable of giving rise in the ordinary way to any thrombosis, either at time of injection or subsequently. Probably the most efficient and safest to use and will remain so until the ideal solution is discovered.—T. H. T. Barber, *Brit. med. J.*, i/1930, 219; *ibid.*, ii/1930, 60.

4 to 10 ml. of 20% solution gives good results, but is not certain in its effects and causes cramp-like pains.—A. H. Douthwaite, "Injection Treatment of Varicose Veins" (H. K. Lewis).

Strong solutions of dextrose (50%) and salt (30%) have gone out of favour, and are only occasionally used in allergic cases.—A. Dickson Wright, *Brit. med. J.*, i/1940, 665.

**Hypotonic Saline Solution (St. G. H.)** is 0.3%.

[P2] **Cheron's Serum.**—Sodium chloride 2, phenol 1, sodium phosphate ( $\text{Na}_2\text{HPO}_4$ , called neutral phosphate in France) 4, sodium sulphate 8, distilled water to 100.

**Enema Sodii Chloridi (B.P.C.).** Dose.—20 ounces (600 ml.). 2.5 to 5% w/v in mucilage of starch or in 5% w/v aqueous soft soap. Hypertonic enema.—4% w/v in water.

**Pulv. Hypertonic (N.I.F.).**

Sodium chloride 4, sodium citrate 1. Two heaped teaspoonfuls to be dissolved in  $\frac{1}{2}$  pt. of warm water.

**Trunecek's Serum** for nervous ailments and high arterial tension.

Dose.—Subcutaneously 1 ml. to commence with, increasing by 0.2 ml. May also be given by rectum and mouth.

Sodium chloride 492, sodium sulphate 44, sodium phosphate 15, sodium carbonate 21, potassium sulphate 40, water to 10,000.

**Tablets of Trunecek's Serum** are prepared 5 grains each, i.e., equivalent approximately to 5 ml. of the serum. Daily dose 3 to 6 with meals. Administration *per os* is equally effective.

For atheroma and sclerosis of arterial coats.

Trunecek's Serum has a freezing point of  $3.29^\circ$ , and an osmotic pressure 5.875 times greater than blood serum—i.e., it is, strongly hypertonic.

[P2] **Acidum Hydrofluoricum.** HF = 20.0. Syn. FLUORIC ACID.

[P1] "*Alkali fluorides other than those specified in Part II of this list.*"

[P2] "*Hydrofluoric acid; potassium fluoride; sodium fluoride; sodium silicofluoride.*"

[S3] "*Sodium fluoride—in substances containing less than 3% of sodium fluoride as a preservative.*"

[S3] "*Sodium silicofluoride—in substances containing less than 3% of sodium silicofluoride as a preservative.*"

Manufactured by the action of sulphuric acid on fluor spar ( $\text{CaF}_2$ ) in lead or platinum vessels, and redistilled for medicinal use. It contains about 40% *w/w* of the gas and emits suffocating fumes. It attacks glass and must be kept in gutta-percha bottles, or bottles coated internally with ceresin or hard paraffin.

#### HYDROFLUORIC ACID BURNS.

Relief from use of copious quantities of dilute ammonia solution followed by ice bath; also, in severe and extensive burns, subcutaneous injection of 10% ammonium chloride solution relieves pain and prevents extension. In from 24 to 48 hours, the areas that have come in contact with acid appear white and lifeless. These areas should be extensively debrided and the white surface tissue removed (this causes no pain). Wet magnesium sulphate dressings are then applied for a few days and subsequently bland ointment dressings. This procedure relieves pain, hastens healing and reduces scarification.—E. E. Evans, *J. Amer. med. Ass.*, ii/1932, 1194.

[P2] **Acidum Hydrofluoricum Dilutum.**

*Dose.*—5 to 15 minims (0.3 to 1 ml.). Contains about 0.5% of the strong acid. Even thus diluted should not be kept in glass bottles. Has been given for goitre.

[P2] **Sodii Fluoridum (B.P.C.).** NaF = 42.00.

*Dose.*— $\frac{1}{2}$  to  $\frac{1}{2}$  grain (0.005 to 0.03 g.), in very dilute solution.

Lustrous cubes or crystalline powder.

*Soluble* 1 in 25 of water, insoluble in alcohol.

**Antidotes.** Wash out the stomach, using lime water or a dilute solution of calcium chloride freely; or give 20 to 30 gr. of calcium chloride or lactate dissolved in water, and then an emetic. The dose of calcium salt should be repeated, or calcium chloride may be given intravenously. Keep patient lying down and warm. Give a purgative dose of castor oil. Demulcent drinks freely. Morphine,  $\frac{1}{2}$  gr. hypodermically, if necessary.

Calcium compounds effective in treatment of fluoride poisoning.—Sharkey and Simpson, *J. Amer. med. Ass.*, i/1933, 100.

Recovery after taking 5½ gr. in the form of an insect powder, mistaken for flowers of sulphur. Sickness, vomiting, diarrhoea, pains in legs and arms, dysphagia, and ocular paralysis with diplopia supervened. Oxygen and stimulants were administered, and later Coramine, strychnine, atropine and radiant heat.—R. D. Bell, *Brit. med. J.*, i/1936, 886.

For references to fluorine in water, see Vol. II.

**Uses.** Given in toxic goitre in doses of 1 dr. of 2% *w/v* solution three times a day with potassium iodide. Given hypodermically as 0.5% *w/v* solution. Mixed with meal is a specific for killing beetles and cockroaches. The aqueous solution attacks glass slowly.

**GRAVES' DISEASE.** 5 ml. of a 2% solution *intravenously* on alternate days. Orally 0.025 g. in pill form. Malaise disappears, pulse rate reduced, weight increases, and B.M.R. lowered. Both exophthalmos and thyroid enlargement

are ultimately much reduced or become unnoticeable. No contraindications and no danger.—L. Goldemberg, per *Brit. med. J. Epit.*, i/1934, 55.

Sodium fluoride does not inactivate thyroxine *in vivo*, but its therapeutic use in hyperthyroidism is not condemned by this finding, since it may have an inhibitory action on the thyroid gland itself.—M. H. Seevers and H. A. Braun, *Proc. Soc. exp. Biol.*, N.Y., 1935, 33, 228.

[P1] **Mistura Sodii Fluoridi (B.V.H.)**. Dose.—1 dr. of A with 1 dr. of B.  
A.—Solution of sodium fluoride (2%) 30 m., aqueous solution of iodine (Lugol's solution) 10 m., water to 1 dr.

B.—Tincture of chloroform and morphine 5 m., tincture of catechu 15 m., syrup 20 m., mucilage of acacia 8½ m., water to 1 dr.

[P1] **Ammonii Fluoridum**. In white deliquescent crystals which attack glass slowly. Has been used in enlargement of the spleen in doses up to ½ gr.

[P2] **Potassii Fluoridum** occurs in deliquescent cubic crystals or as a crystalline powder. It attacks glass slowly.

**Quininae Hydrofluoridum**.  $C_{20}H_{24}O_2N_2.HF = 344.2$ .

Dose.—1 to 2 grains (0.06 to 0.12 g.). Has been recommended for use in exophthalmic goitre.

[P2] **Sodii Silicofluoridum (B.P.C.)**. Syn. SODIUM FLUOSILICATE.  $Na_2SiF_6 = 188.1$ .

Fine white granular or crystalline powder, becoming gelatinous when moist. **Soluble** about 1 in 200 of water, giving a turbid acid solution. The 1 in 500 solution is non-caustic and has been used as an external antiseptic. Concentrated solutions attack metal and porcelain enamel.

Useful as an insecticide, being both a contact and stomachic poison. It has the advantages over arsenicals of cheapness, more rapid killing, and of effectiveness against a wide range of insects. Mixed with 9 parts of hydrated lime, it has been successfully used as a field dust against many pests.

For insects and lower organisms, e.g., worms and protozoa, sodium fluosilicate is more toxic than sodium arsenite. To man and the higher animals the arsenicals are 9 times more toxic than sodium silicofluoride and 30 times more toxic than sodium fluoride.

Two fatal cases of poisoning. Sodium silicofluoride is commonly sold as an insect powder. Half a spoonful, taken in mistake for carbonate, caused death in 10 hours.—*Chem. Zeit.*, 1925, 805, per *Analyst*, 1926, 313.

## ACIDUM HYDROCYANICUM

HCN = 27.02.

[P1] "*Hydrocyanic acid; cyanides; double cyanides of mercury and zinc.*"

[S1] "*Hydrocyanic acid except substances containing less than 0.15%, weight in weight, of hydrocyanic acid (HCN); cyanides except substances containing less than the equivalent of 0.1%, weight in weight, of hydrocyanic acid (HCN); double cyanides of mercury and zinc.*"

[S6] "*Hydrocyanic acid; cyanides; double cyanides of mercury and zinc*"—specify proportion in a preparation as the proportion of hydrocyanic acid (HCN) that the preparation would be calculated to contain on the assumption that the cyanides in the poison had been wholly converted into hydrocyanic acid."

Rule 20 (2). "It shall not be lawful to sell or supply any compressed hydrocyanic acid unless the container is labelled with the words 'Warning. This container holds poisonous gas and should



only be opened and used by persons having expert knowledge of the precautions to be taken in its use.''' (Note: this rule is additional to other rules which apply to hydrocyanic acid and other poisons generally.)

[P1-S1] **Acidum Hydrocyanicum Fortius** (B.P.C.). *Syn.* SCHEELE'S HYDROCYANIC (or PRUSSIC) ACID.

*Dose.*—1 to 3 minims (0.06 to 0.2 ml.).

Manufactured by distillation of potassium ferrocyanide with dilute sulphuric acid.

A colourless liquid with powerful odour. Sp. gr. about 0.994. Contains approximately 4% HCN.

**Antidotes.** Give emetic immediately (may not be effective). Empty stomach by stomach tube, using 60 gr. of potassium permanganate in 2 gallons of water. Give, as chemical antidote, 15 gr. of ferrous sulphate, 20 m. of solution of ferric chloride and 1 to 2 dr. of magnesium carbonate mixed with a wineglassful of water; repeat this dose as required. Hydrogen peroxide, diluted about 1 in 16, may also be used. Artificial respiration, kept up steadily (20 per minute); oxygen, or oxygen and carbon dioxide (7%) inhalations. Ammonia inhalations. Stimulants, e.g., strychnine,  $\frac{1}{8}$  gr., or caffeine sodium benzoate, 2 gr., hypodermically. Intravenous injection of sodium thiosulphate, 10 to 50 ml. of 20% solution, or methylene blue, 50 ml. of 1% solution.

Review of cases of cyanide poisoning; antidotes most satisfactory seem to be sodium nitrite and sodium thiosulphate intravenously, and amyl nitrite by inhalation.—Chen, Rose and Clowes, *J. Amer. pharm. Ass.*, 1935, 625.

Hydrocyanic acid used in industry, gilding, dyeing, fumigation, etc.; it has been stated that no man should be without protection unless concentration of gas is less than 0.01%, and for long exposures concentration should be much lower than this.

In ridding a house of bed-bugs it cannot be too strongly emphasised that fumigation by hydrogen cyanide is a dangerous process and should be undertaken only by responsible persons with full knowledge of the nature and properties of the gas, and who are skilled in the use of gas masks and oxygen breathing apparatus. In order to minimise risk, a lachrymating gas may be mixed with hydrogen cyanide to act as an indicator. Failure to detect the lachrymating gas, however, can of itself be accepted neither as indicating the absence of hydrogen cyanide nor that ventilation is complete.—*Rep. med. Offr. Minist. Hlth, Lond.*, 1934, 161.

Recovery from two cases of cyanide poisoning is reported after treatment with sodium nitrite and sodium thiosulphate intravenously.—A. P. Ingegno and S. Franco, per *J. Amer. pharm. Ass.*, 1938, 335.

[P1-S1] **Acidum Hydrocyanicum Dilutum** (B.P., P. Ned. V, P. Belg. IV). *Syn.* DILUTE PRUSSIC ACID.

*Dose.*—2 to 5 minims (0.12 to 0.3 ml.). *Fr. Cx.*—Max. single dose  $1\frac{1}{2}$  minims, max. during 24 hours 8 minims.

Contains 2% w/w of HCN, sp. gr. about 0.997. Keep in inverted stoppered bottles in the dark.

**Incompatible** with soluble salts of silver, mercury and iron.

**Uses.** In dyspepsia with pain, combined with bismuth or sodium bicarbonate. It is very useful as a sedative in an effervescent mixture. Dilute hydrocyanic acid 5 minims in 2 drachms of water is useful to allay vomiting and cough.

[P1] **Lotio Acidi Hydrocyanici et Bicarbonatis** (L.H., R.L.O.H.).

Dilute hydrocyanic acid 5 m., borax 4 gr., sodium bicarbonate 4 gr., sterilised water to 1 oz. A soothing eye lotion.

[P1-S1] **Potassii Cyanidum** (B.P.C.). *Syn.* POTASSIUM CYANURET (an old name), KALIUM CYANATUM, CYANKALI, CYANURE DE POTASSE. KCN = 65.10.

*Dose.*— $\frac{1}{12}$  to  $\frac{1}{4}$  grain (0.005 to 0.016 g.).

A crystallised salt or in fused masses, deliquescent and decomposed on exposure to air.

*Soluble* 1 in  $2\frac{1}{2}$  of water, 1 in 10 of alcohol 90%.

*Antidotes.* See under Acidum Hydrocyanicum Fortius, p. 71.

**TRADE VARIETIES.** Commercial fused potassium cyanide is obtainable in various strengths, equivalent to 30, 40, and 90 to 95% of KCN; is also obtainable as a mixture with sodium cyanide containing the equivalent of 98 to 100% of KCN; "gold cyanide," for gold extraction. 30% pure is supplied in sticks; this is "silver cyanide," for silver extraction. Sodium cyanide is equivalent to 130% of KCN.

**Potassium Cyanate**, KCNO, is made by oxidising potassium cyanide with red lead. Colourless crystals readily soluble in water.

**Potassii Ferricyanidum.**  $K_3Fe(CN)_6$  = 329.2. Red crystals. Used as a reagent and in photography.

A fatal case of poisoning by potassium ferricyanide, the first recorded for many years.—H. W. Greenwood, per *Chem. & Drugg.*, ii/1940, 139.

**Potassii Ferrocyanidum.**  $K_4Fe(CN)_6 \cdot 3H_2O$  = 422.3. In lemon-yellow crystals.

*Dose.*—8 grains (0.5 g.). Said to be physiologically almost without action.

**Potassii Thiocyanas.** *Syn.* POTASSIUM SULPHOCYANIDE, POTASSIUM RHODANIDE. KSCN = 97.17.

*Dose.*— $\frac{1}{2}$  to 3 grains (0.05 to 0.2 g.).

Made by fusing potassium cyanide with sulphur.

**Uses.** There is a similarity between the actions of the thiocyanates and the iodides and the toxic symptoms are similar to those of iodism. Mainly used in hypertension, but in view of the toxic effects the justification of this therapy is doubtful. Treatment may begin with  $1\frac{1}{2}$  gr. three times a day, and the dose decreased or increased (up to 15 gr. per day) as required.

In the treatment of uncomplicated vascular hypertension in patients under 60 years of age it has decided value, but patients must be closely watched, and if a patient fails to respond at blood-cyanate levels of 12 to 14 mg. per 100 ml., maintained for 2 to 4 weeks (higher concentrations may be very dangerous), the treatment should be stopped. In 75 patients treated minor toxic symptoms occurred in 23 and serious complications in 6.—R. W. Robinson and J. P. O'Hare, *New Engl. J. Med.*, ii/1939, 964.

There is no clear evidence as to its clinical value in essential hypertension, and its hypotensive effect is almost always accompanied by *distressing side reactions* (weakness, fatigue, drowsiness, and gastro-intestinal symptoms) whether given in large doses for short periods or small doses for long periods. Arteriosclerosis a contraindication.—D. Ayman, *J. Amer. med. Ass.*, i/1931, 1857. Both sodium and potassium thiocyanates produced *very disagreeable side-effects*.—W. C. Egloff and co-workers, *ibid.*, 1942.

Exfoliative dermatitis following use of  $1\frac{1}{2}$  grains three times daily for a week.—C. R. Weis, *J. Amer. med. Ass.*, ii/1929, 988. Acute diffused erythematous dermatitis caused.—*Brit. med. J. Epit.*, ii/1929, 96.

**Sodii Thiocyanas.** *Syn.* SODIUM RHODANIDE, SODIUM SULPHOCYANIDE. NaCNS = 81.1.

*Dose.*—1 to 5 grains (0.06 to 0.3 g.), up to 15 grains (1 g.) daily.

A crystalline colourless salt, soluble in water 1 in 0.3 and 1 in 0.6 of alcohol 90%. Has been employed in hypertension in a similar manner to the potassium salt. The dose usually recommended is 2½ gr. twice or thrice daily after meals in an aromatic mixture. Up to 15 gr. daily tolerated over a period of 3 weeks.

The toxic and therapeutic effects of thiocyanates are often very close together and there are few indications that they are in any way superior, or even equal, to the older vasodilators.—*Lancet*, ii/1932, 1169.

Forty-five patients with hypertension were given sodium or potassium thiocyanate and the concentration of the cyanates in their blood followed. The reduction of blood pressure and the relief of symptoms obtained in thirty-five roughly corresponded to the level of the cyanates in the blood. The optimum therapeutic level would seem to range between 8 and 12 mg. per 100 ml., and significant toxicity begins to appear at from 15 to 30 mg. The individual tolerance varies greatly, the different levels being obtained with widely varying doses. The cyanates may reach hazardous concentrations very quickly in some individuals, so that the administration of the thiocyanates is believed to be dangerous unless controlled by close observation and blood cyanate determinations.—M. H. Barker, *J. Amer. med. Ass.*, i/1936, 766.

Toxic manifestations of the thiocyanates.—M. H. Wald *et al.*, *J. Amer. med. Ass.*, i/1939, 1120. Fatalities.—C. F. Jarvin, *ibid.*, 1125.

**Elixir Sodium Sulphocyanate** (*Duncan, Flockhart, Edinburgh*). Each fl. dr. contains 2½ gr. of sodium sulphocyanate. *Dose.*—1 to 2 teaspoonfuls. In arterial hypertension.

**Rhodopurin** (*Camden Chemical Co., London*). Caffeine-thiocyanammonia in 5-grain tablets. Arterial hypertension.

[P1-S1] **Laurocerasus** (B.P.C.). *Syn.* CHERRY-LAUREL. The fresh leaves of *Prunus Laurocerasus* (Rosaceæ).

[P1] **Aqua Laurocerasi** (B.P.C., *Fr. Cx., P.G. V, P. Helv. V*).

*Dose.*—½ to 2 drachms (2 to 8 ml.). Standardised to 0.1% of HCN. *P. Helv. V* requires this to be dispensed when Aqua Amygdalæ is prescribed.

## ACIDUM HYPOPHOSPHOROSUM .

B.P.C., U.S.P. XI.

$H_3PO_2 = 66.0$ .

*Dose.*—2 to 5 minims (0.12 to 0.3 ml.). U.S.P. XI average dose 3 minims.

A monobasic acid occurring as a colourless liquid containing 30 to 32% w/w of  $H_3PO_2$ . Sp. gr. about 1.14.

**Antidotes.** Give copper sulphate as emetic, or use the stomach tube with dilute solution of potassium permanganate.

**Acidum Hypophosphorosum Dilutum** (B.P.).

*Syn.* ACIDUM HYPOPHOSPHOROSUM (F.E. VIII).

*Dose.*—5 to 15 minims (0.3 to 1 ml.).

Contains 10% w/w of  $H_3PO_2$ . It may be prepared by diluting 323 g. of the B.P.C. concentrated acid with 677 g. of water (approximately 5 fl. oz. 440 m. to 1 pint).

**Uses of Hypophosphites.** There is no reliable evidence that the hypophosphites exert any physiological effect. They are stated to be excreted unchanged in the urine, and any benefit may be

ascribed to the base with which the acid is combined. Hypophosphites are prescribed as a nerve tonic in anæmia and neurasthenia and also in disturbed nutrition and wasting diseases.

**Calcii Hypophosphis** (*B.P.C.*, *P. Helv. V*, *Fr. Cx.*).

$\text{Ca}(\text{H}_2\text{PO}_3)_2 = 170.07$ .

*Dose.*—3 to 10 grains (0.2 to 0.6 g.).

White crystalline salt, with nauseous taste, soluble 1 in 8 of water, insoluble in alcohol 90%. Prepared by heating phosphorus with milk of lime until phosphoretted hydrogen ceases to be given off, filtering and evaporating or precipitating with alcohol to crystallise.

**Incompatible** with oxidising agents.

**Syrupus Calcii Hypophosphitis** (*B.P.C.*).

*Dose.*—1 to 4 drachms (4 to 16 ml.). Contains 1 grain per drachm.

**Ferri Hypophosphis** (*B.P.C.*).  $\text{Fe}(\text{H}_2\text{PO}_3)_3 = 250.9$ .

*Syn.* FERRIC HYPOPHOSPHITE.

*Dose.*—1 to 3 grains (0.06 to 0.2 g.) in a pill or cachet.

Whitish amorphous powder with a chalybeate taste, and containing about 22% of Fe. Slightly **soluble** in water, but more so in presence of potassium citrate, or of hypophosphorous acid.

**Liquor Ferri Hypophosphitis** (*B.P.C.*).

*Syn.* LIQUOR FERRI HYPOPHOSPHITIS FORTIS.

*Dose.*—10 to 30 minims (0.6 to 2 ml.).

[P1-81] **Pilula Ferri Hypophosphitis cum Strychnina**. Strychnine,  $\frac{1}{10}$  gr., ferric hypophosphite 2 gr. To make one pill (or in grammes to make 15).

*Dose.*—1 twice or thrice daily.

**Syrupus Ferri Hypophosphitis** (*B.P.C.*).

*Dose.*— $\frac{1}{2}$  to 2 drachms (2 to 8 ml.).

Solution of iron hypophosphite 1, syrup to 5.

**Magnesii Hypophosphis** (*B.P.C.*).

$\text{Mg}(\text{H}_2\text{PO}_3)_2 \cdot 6\text{H}_2\text{O} = 262.5$ .

*Dose.*—3 to 10 grains (0.2 to 0.6 g.). White crystalline salt **soluble** about 1 in 5 of water.

**Potassii Hypophosphis** (*B.P.C.*).  $\text{KH}_2\text{PO}_3 = 104.1$ .

*Dose.*—3 to 10 grains (0.2 to 0.6 g.).

A deliquescent granular white powder, having a nauseous, bitter taste. **Soluble** 1 in 0.6 of water, 1 in  $7\frac{1}{2}$  of alcohol 90%.

**Incompatible** with oxidising agents.

**Sodii Hypophosphis** (*B.P.C.*, *Fr. Cx.*).  $\text{NaH}_2\text{PO}_3 = 88.03$  (+ $\text{H}_2\text{O}$  *P. Ned. V*; about 1  $\text{H}_2\text{O}$  *P. Helv. V* and *P. Dan.*).

*Dose.*—3 to 10 grains (0.2 to 0.6 g.).

A white granular deliquescent salt, with a bitter, nauseous taste. **Soluble** 1 in 1 of water, and 1 in 30 of alcohol. Explosive when mixed with nitrates or other oxidising agents.

**Fosfoxy** (*Anglo-French Drug Co., London*). Sodium salt of hypophosphomonoterebinic acid, obtained by the combination of phosphorus and turpentine. Supplied as syrup or pills. *Dose.*—One teaspoonful of syrup, or 2 pills, three or four times daily. In neurasthenia, anæmia, etc.

**Extractum Malti cum Hypophosphitibus** (*B.P.C.*).

Liquid extract of malt with  $\frac{1}{4}$  gr. each of sodium and calcium hypophosphites per dr.

[P1] **Glycerinum Hypophosphitum Compositum (B.P.C.).**

*Syn.* GLYCEROL HYPOPHOSPHITIS.

*Dose.*—1 to 2 drachms (4 to 8 ml.).

Contains the hypophosphites of calcium, potassium, manganese and quinine with about  $\frac{1}{80}$  gr. of strychnine per dr. It is free from sugar.

[P1] **Syrupus Hypophosphitum Compositus (B.P.C.).**

*Syn.* SYRUPUS FERRI HYPOPHOSPHITIS COMPOSITUS.

*Dose.*—1 to 2 drachms (4 to 8 ml.).

Contains the hypophosphites of calcium, potassium, manganese, and quinine with about  $\frac{1}{80}$  gr. of strychnine per dr.

[P1] **Tabellæ Hypophosphitum Compositæ (B.P.C.)** are each equivalent to 1 drachm of the compound syrup.

## ACIDUM LACTICUM

*B.P., U.S.P. XI, Fr. Cx., P. Helv. V, etc.*



*Dose.*—5 to 20 minims (0.3 to 1.2 ml.), well diluted.

A colourless, odourless, syrupy, sour liquid, obtained by the fermentation of milk sugar by the action of *Bacillus acidi lactici*. Lime or zinc oxide is used to neutralise the acid as formed. The respective lactates are then decomposed. It has sp. gr. about 1.21 and consists of a mixture of hydrogen lactate and lactide ( $\text{C}_6\text{H}_8\text{O}_4$ ) containing the equivalent of not less than 87.5% of  $\text{C}_3\text{H}_5\text{O}_3$ .

*Fr. Cx.* has sp. gr. 1.23 at 15°.

**Solubility.** Is miscible with water, alcohol and ether; it coagulates milk and albumin.

**Antidotes.** Empty stomach by stomach tube, using lime water. Give doses of magnesia stirred up in water (or chalk or magnesium carbonate, if magnesia is not available). Demulcent drinks.

**Uses.** It has been used locally in tuberculous ulceration of the pharynx and larynx (50% solution), in diphtheria, etc., and internally for infantile and tropical diarrhoea, dyspepsia, as a stomachic tonic in combination with iron and calcium, and in vesical catarrh. Chronic enteritis has been treated by lactic acid  $7\frac{1}{2}$  minims thrice daily after meals. A 1 in 10 solution is used as a douche in leucorrhœa. A 1 in 3 dilution has been recommended as an application in alopecia. As a paint, or paste with kaolin, or as a 50% injection, it has been used in lupus, but is painful. It is a constituent of some contraceptive pessaries and jellies.

**ARTHRITIS.** In cases of traumatic arthritis injection of lactic acid restores functional activity. The formula of the injection is as follows: procaine hydrochloride 2 g., sodium chloride 0.5 g., lactic acid N/5 0.2 ml., water to 100 ml. This solution has an acidity of pH 5. The amount injected is 2 ml. for elbow and ankle-joint cases and 4 ml. for shoulder-joint cases. The treatment should be reserved for cases showing severe disorganisation of joints.—W. G. Waugh, *Lancet*, i/1938, 487.

**Lactic Acid Milk** consists of fresh milk to which lactic acid 1 dr. has been added drop by drop to each pint of milk. It is used for infant feeding and in gastro-enteritis.

**Hydrochloric Acid Milk** is made similarly, using 40 m. of dilute hydrochloric acid. It is used in lactalbumin sensitisation, especially for the eczema and asthma of children. In cases of malnutrition or infection the gastric juice tends to contain less acid; acid milk is therefore particularly useful in such cases.

**Acidum Lacticum Dilutum (B.P.C.).**

*Dose.*— $\frac{1}{2}$  to 2 drachms (2 to 8 ml.).

Lactic acid 174.5 g., distilled water to 1000 g. (approximately 3 fl. oz. to 1 pint). Contains about 16% w/w of  $C_3H_5O_3$ . Sp. gr. about 1.04.

**Limonade Lactique (Fr. Cx.).** Dilute lactic acid 4, water 86, simple syrup 10, all by weight.

**Pessus Acidi Lactici (B.P.C.)** contain  $2\frac{1}{2}$  m. of acid in 30 gr. of oil of theobroma.

[P2] **Pigmentum Acidi Lactici cum Phenole (Mid. H.).**

Liquefied phenol 120 m., lactic acid to 1 oz. For lupus erythematosus.

**Koromex (Holland-Rantos Co., New York; Prentif Ltd., London).** Contractive jelly stated to contain boric, lactic and stearic acids and a stabiliser.

**Syrupus Acidi Lactici (B.P.C.).**

*Dose.*—1 to 2 drachms (4 to 8 ml.).

Lactic acid  $2\frac{1}{2}\%$  v/v in syrup.

**Calcii Lactas (B.P., U.S.P. XI, Fr. Cx., etc.).**

$(CH_3 \cdot CHO \cdot COO)_2Ca, 5H_2O = 308.2$ .

*Dose.*—15 to 60 grains (1 to 4 g.). *Intravenously*, 5 to 10 grains (0.3 to 0.6 g.) well diluted has been suggested. *Subcutaneously* too irritating. U.S.P. XI average dose is 15 grains.

**Solubility.** Samples vary in solubility, two kinds being obtainable. One has a solubility of 1 in 20 at  $23^\circ$ , and the other 1 in 16.—N. Glass, *Quart. J. Pharm.*, 1933, 522.

The B.P. gives 1 in 18.5 (at  $15^\circ$ ). The solubility does not decrease with age. Slightly soluble in cold alcohol; soluble in boiling alcohol; insoluble in ether.

An opaque white crystalline powder.

**Uses.** Urticaria and chilblains have been treated with it. Chilblains are stated to be caused by a slow coagulation rate of the blood, which permits of effusion into the tissues and consequent swelling and inflammation. May be given in 15 gr. doses in chloroform water 1 oz., three times a day one hour before meals, to be continued over 6 weeks. Has been found of value in metrorrhagia. Is given during pregnancy (in conjunction with vitamin D) to replace calcium taken by the fœtus and to improve tone of involuntary muscle. Migraine is stated to be aborted by the taking of 30 grains at the first warning of onset.

Children in a nursing school in South India were given 0.5 g. of calcium lactate daily, and showed greater increases in height and weight during a 4 to 5 month period than children not receiving the supplement. The acceleration in growth was accompanied by an improvement in general condition. Supplements of calcium salts are recommended as a milk substitute when milk cannot be supplied.—W. R. Aykroyd and R. S. B. Krishnan, *Lancet*, ii/1938, 153.

**Liquor Calcii Lactatis (B.P.C.).**

*Dose.*—1 to 4 drachms (4 to 16 ml.) or more. Contains the equivalent of about 10 gr. of calcium lactate in 4 dr.

*Mist. Calc. Lact. (N.I.F.).* Calcium lactate 10 gr., syrup 30 m., chloroform water to  $\frac{1}{2}$  oz.

**Mistura Calcii Lactatis (W.H.).**

Calcium lactate 15 gr., sodium lactate 5 gr., spirit of chloroform 5 m., water to  $\frac{1}{2}$  oz.

*Tabellæ Calcii Lactatis (B.P.C.)* contain 5 gr. (0.3 g.).

**Tabellæ Parathyroidei et Calcii Lactatis (B.P.C.).**

*Dose.*—1 to 4 tablets. Contain 5 gr. of calcium lactate and  $\frac{1}{10}$  gr. of parathyroid.

**Calcii Lactas Recens.** The lactide does not interact unless the reactants are heated. A solution containing 100 gr. of calcium lactate is obtained by boiling for 20 minutes calcium carbonate 40 gr. with lactic acid 1 dr. diluted with 10 dr. of water, the diluted acid being added slowly to the carbonate. The product is filtered, the residue washed and the filtrate and washings diluted to volume.—*Pharm. J.*, ii/1930, 515.

**Calcii et Sodii Lactas (B.P.C.).**

$\text{Ca}(\text{C}_3\text{H}_5\text{O}_3)_2, 2\text{NaC}_3\text{H}_5\text{O}_3, 4\text{H}_2\text{O} = 514.3.$

*Dose.*—5 to 30 grains (0.3 to 2 g.).

White powder or granules containing 8.5 to 9.5% of Ca, 10 to 11% of Na calculated on the dried substance, and not more than 16% of moisture.

Used for the same purposes as calcium lactate. The presence of sodium lactate is stated to increase the solubility and ease of absorption.

*Tabellæ Calcii et Sodii Lactatis (B.P.C.)* contain  $7\frac{1}{2}$  gr. (0.5 g.).

**Tabellæ Parathyroidei et Calcii et Sodii Lactatis (B.P.C.).**

*Dose.*—1 to 4 tablets.

Contain  $7\frac{1}{2}$  gr. of calcium sodium lactate and  $\frac{1}{10}$  gr. of parathyroid.

**Calsolact (Allen & Hanburys, London).** Tablets contain  $7\frac{1}{2}$  gr. of calcium sodium lactate.

**Kalsolac (Evans, Sons, Lescher & Webb, Liverpool).** Capsules containing calcium lactate 78.05%, iron lactate 19.51%, and magnesium lactate 2.44% with 500 i.u. of vitamin D for the prevention and treatment of chilblains.

**Kalzana Tablets (Wulff, Berlin; Therapeutic Products, London)** are stated to contain  $3\frac{1}{2}$  gr. each of calcium lactate and sodium lactate.

**Nutritive Salts (Parke, Davis, London).** A combination of salts of calcium, magnesium, sodium, potassium, manganese, iron, etc., in 15 gr. tablets. For supplementing the diet in respect of mineral constituents, and preventing acidosis.

**Calcii Lactophosphas.**

*Dose.*—3 to 8 grains (0.2 to 0.5 g.).

Hygroscopic, crystalline powder. Some samples have consisted of a mixture of equal parts of calcium lactate and (dibasic) calcium phosphate. **Soluble** in water. A stomachic tonic especially useful for children.

**Liquor Calcis Lactophosphatis.** Rub dibasic calcium phosphate 17, smoothly with water 964, add lactic acid 19—all by weight. Shake to dissolve; filter.

**Calcium Lactophosphoricum Solutum** (*Fr. Cx.*). Calcium lactate 33 g. is shaken with phosphoric acid 19 g., in a little water and made up to 1000 g. after filtration.

**Syrupus Calcii Lactophosphatis** (*B.P.C.*).

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Contains the equivalent of 4 gr. calcium lactate per drachm.

**Dusart's Syrup.** *Dose.*—2 drachms to  $\frac{1}{2}$  ounce (8 to 15 ml.).

Calcium carbonate 9, lactic acid 75% 22, phosphoric acid 10% 88, water *q.s.* Dissolve the calcium carbonate in the lactic acid diluted to 108 with water with the aid of heat. Cool and add the phosphoric acid, and make up to 370. Dissolve in this sugar 623, and add spirit of limes 7. Mix and adjust to 1000. *All parts by weight.*

**Syrupus Calcii Lactophosphatis cum Ferro** (*B.P.C.*).

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Contains  $\frac{1}{2}$  gr. of ferrous lactate with potassium citrate and water in syrup of calcium lactophosphate to 1 dr.

**Ferri Lactas** (*B.P.C., Fr. Cx., P. Belg. IV, P. Ital. V, P. Jap., P. Dan., P. Helv. V, Ph. Ned. V, F.E. VIII.*) *Syn.* FERROUS LACTATE.  $(C_3H_5O_3)_2Fe, 3H_2O = 288.0$ .

*Dose.*—1 to 5 grains (0.06 to 0.3 g.).

In greenish white crystals with characteristic odour. *Soluble* 1 in 40 of water; readily soluble in alkali citrate solutions; when taken internally is easily assimilated by the system.

**Potassii Lactas.**  $C_3H_5O_3K = 128.0$ .

*Dose.*—5 to 15 grains (0.3 to 1 g.). Occurs as a syrupy liquid or as a very deliquescent amorphous mass soluble in water and alcohol 90%.

**Sodii Lactas.**  $C_3H_5O_3Na = 112.0$ .

*Dose.*—5 to 10 grains (0.3 to 0.6 g.).

Usually in form of colourless or yellowish syrupy liquid miscible with water, containing 70% of the salt.

**Uses.** Is given intravenously as an isotonic ( $\frac{1}{2}$  molar) solution in all types of severe acidosis other than that associated with congenital heart disease with persistent cyanosis, and for rapid alkalisation of the urine in the treatment of urinary infections. Its use has been recommended, in 40-grain doses thrice daily, in diabetes mellitus when there is a tendency to acidosis.

The administration of sodium lactate prior to the use of chloroform has been suggested to prevent possible acidæmia. In other forms of acidosis the chief indication is when the  $CO_2$  content of the blood is below 25 vols. per cent., when the dose should be 60 ml. per kg. body weight. For alkalisation of urine, 30 ml. per kg. body weight.

A concentrated (molar) stock may be made by neutralising 100 ml. of lactic acid with concentrated (about 40%) carbonate-free sodium hydroxide using phenol red as indicator, diluting to 800 ml. and boiling for 30 to 40 minutes, more alkali being added as necessary to neutralise the lactic acid produced by hydrolysis of lactide. The solution is diluted to 1000 ml., filtered and autoclaved at 15 to 20 lb. pressure for 30 minutes. For use this solution is diluted with five times its volume of sterile water.

Sodium lactate is suggested as a substitute for glycerin, which it may replace in Kaolin poultice.



**Lactate-Ringer Solution.** *Syn.* HARTMANN'S SOLUTION.

Add 10 ml. of concentrated (molar) sodium lactate solution to from 400 to 450 ml. of modified hypotonic Ringer's Solution (containing sodium chloride 6 g., potassium chloride 0.4 g., calcium chloride 0.2 g., magnesium chloride 0.2 g., water to 1000 ml.).

For all types of dehydration. Indicated especially for counteracting acidosis when sufficient sodium bicarbonate cannot be added to Ringer's Solution because of precipitation of calcium bicarbonate. *Dose.*—80 to 100 ml. per kg. body weight. In gastro-enteritis in infants the solution rapidly checks the vomiting, but not the diarrhoea.

With 10% dextrose it is the fluid of choice for the continuous intravenous drip method.—A. F. Hartmann, *J. Amer. med. Ass.*, ii/1934, 1349.

**Physiological Buffer Solution (Hartmann Solution) (Lilly, London).**

*Dose.*—For children up to one year 250 ml. of diluted solution; for children from 1 to 8, up to 1000 ml.; subcutaneously, intraperitoneally or intravenously, in amounts sufficient to maintain elasticity of skin. Before using, the solution is diluted 25 times with freshly distilled water or glucose solution.

Not more than 30 ml. per kilo bodyweight is given. Indicated in dehydration with alkalosis or acidosis.

**Strontii Lactas (Fr. Cx.).**  $(C_2H_5O_2)_2Sr, 3H_2O = 319.8$ .

*Dose.*—5 to 30 grains (0.3 to 2 g.).

A white crystalline powder, very soluble in water, of service in albuminuria and Bright's disease. May be combined with iron in the albuminuria of pregnancy. To increase coagulability of the blood 15 to 30 grain doses useful.

Tetany can be prevented or relieved by the continuous oral administration of strontium lactate. It acts by decreasing the permeability of the gut to calcium excretion and by reducing the excitability of the motor nerves.

**Tabletæ Strontii Lactatis Compositæ (G.H.).** Each tablet contains strontium lactate  $\frac{1}{2}$  gr., lithium citrate  $\frac{1}{2}$  gr., caffeine citrate  $\frac{1}{2}$  gr., quinine sulphate  $\frac{1}{2}$  gr., sodium benzoate 1 gr., excised magnesium sulphate 2 gr., excised sodium sulphate 8 gr.

**Zinci Lactas.**  $(C_2H_5O_2)_2Zn, 3H_2O = 297.5$ .

*Dose.*— $\frac{1}{2}$  to 3 grains (0.03 to 0.2 g.). Max. *pro die* 10 grains. (Has been used in France up to 3 g. for a dose.—Dorvault.)

White crystals soluble 1 in 60 of water. In epilepsy.

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## ACIDI LACTICI BACILLI

To arrest the growth of putrefactive organisms in the intestines and to stimulate intestinal digestion and diminish toxic absorption from the bowel, Metchnikoff proposed the acclimatisation of the lactic acid bacillus. He concluded that, as organisms of putrefaction only increase with difficulty in neutral or acid media, the most feasible procedure would be to introduce a lactic acid organism (growing in a sugar medium) into the human being to arrest the proliferation of harmful bacteria. For this purpose he chose the bacillus known as the Bulgarian Bacillus (*B. Caucasicum*), which occurs in natural soured milk, as being the best acid producer.

*B. Caucasicum* is not, however, a normal inhabitant of the intestinal tract, and in spite of Metchnikoff's claims to the contrary, later workers found it very difficult to produce a growth of this organism in the intestines. Various other acid-forming bacteria have therefore been employed, of which the one most favoured is *B. acidophilus*. This is a normal inhabitant of the human intestine, and is the organism best adapted to the purpose of maintaining the intestinal flora in a healthy condition, since it survives and multiplies with ease.

The taking of cultures of this organism, usually in the form of *B. acidophilus* milk, combined with the liberal consumption of lactose or dextrin, the carbohydrates most favourable to its growth, is the best procedure for supplanting the putrefactive organisms of the intestine with fermentative ones. The patient should first go on an exclusive diet of *B. acidophilus* milk (1 to 2 quarts daily) for a week, with 2 to 3 ounces daily of lactose, after which cereals, fruits and vegetables in liberal amounts should be added to the diet and protein-rich foods omitted for several weeks.

Although this form of therapy has been advocated in a wide variety of conditions, including skin disorders such as eczema and psoriasis, intestinal tuberculosis and cancer of the stomach, it is most successfully employed in the summer diarrhoea of children, in infective conditions of the intestinal tract, and in enteritis and colitis generally; obstinate constipation in adults is also said to be relieved by daily doses of *B. acidophilus* milk, which are also stated to be of value in sprue.

Lactic acid bacilli are supplied commercially in three forms: (1) as living cultures in broth, whey or whole milk, but the bacteria in these cultures only remain viable for a few days, and the cultures require to be kept in a refrigerator; (2) as tablets, but the bacteria do not retain their viability for any length of time in the dry state, and most tablets of this type contain no living organisms; (3) as chocolate-coated agar-jelly blocks, but these are unstable and must bear an expiry date.

#### **Lac Coactum (B.P.C.).**

Curdled milk is prepared by sterilising cows' milk by heating it in an autoclave at 125° for 30 minutes and cooling to 40°. A culture of *B. Caucasicum* or *B. acidophilus* is then added, and the temperature maintained at 38° to 40° for 8 to 12 hours. The milk, when ready for consumption, is in the form of a junket.

**Koumiss (Artificial).** Dissolve dextrose  $\frac{1}{4}$  ounce in water 4 ounces, and add 20 grains of yeast and cows' milk 4 ounces. Place in a quart bottle and fill up with milk; cork and wire. Keep it cool and shake it frequently during 4 days. Koumiss thus prepared contains some alcohol (1 to 2%) and lactic acid (about 1 to 2%). The original koumiss of the Tartars was made from mares' milk by using the Kephir ferment, which swells up on soaking in milk. This consisted in reality of yeast cells with certain bacteria (*B. Caucasicum*, Kern). It is a food used in the Caucasus as a stimulant.

**Yoghourt.** *Preparation*—Raise the milk to boiling point. Remove from the heat and cool enough for a skin to form on top. While still too hot to be held conveniently inoculate by allowing some previous Yoghourt—thinned with sterile water, if necessary—to slip down the edge of the container all round the rim. Cover, and, without shaking, place in a closely fitting hay-box until the next day. Do not allow to cool before placing in hay-box.

In Greece Yoghourt is much in use both as a food and for treatment. It is prepared there by adding a little lemon-juice to fresh milk, which is kept warm for 8 hours, forming a curd. From the curd a tablespoonful is mixed with boiled milk, and this procedure is repeated several times, with fresh milk on each occasion, until a Yoghourt of suitable consistency is obtained. Small spoonfuls of this latter product are added to wooden or earthenware pans containing milk which has been boiled and is still slightly warm. This forms the commercial Yoghourt, which curdles in 4 hours at 35°. In order to keep it, and this one may do for as long as from 5 to 8 days, it is poured into little bags of cotton from

which the whey filters, the products thereby becoming thicker and of better keeping qualities.

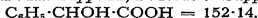
**Lactobacilline** (*Darrasse, Nanterre; Wilcox, Jozeau, London*), **Sauerin** (*Allen & Hanburys, London*), and **Trilactine** (*Martindale, London*) are commercial preparations of lactic acid bacilli.

**Buttermilk** contains protein 3, fat 0.5, sugar 4.8, water 91 per cent. The ordinary lactic acid bacilli found in this are not so active or resistant as those contained in Bulgarian sour milk. Milk in any form, however, in sufficiently large quantity tends to lessen internal putrefaction. Erysipelas has been treated by buttermilk internally and locally.

**Buttermilk Powder** (G.L.) (*Glaxo Laboratories, London*) is milk from which greater part of fat is removed and some lactose has fermented. Contains lactose 42%, protein 33.5%, fat 3.5%, lactic acid 6.5%, water 3.5%, etc. When reconstituted it gives a solution of pH 5 and acts as a buffered "acid-sparer," for use in the diarrhoeal diseases of infants.

## ACIDUM MANDELICUM

*U.S.P. XI Supp. II, P. Ned. V Supp. II.*



*Syn.  $\alpha$ -HYDROXYPHENYLACETIC ACID, PHENYLGLYCOLLIC ACID.*

*Dose.*—45 grains (3 g.) in 1 oz. of water, neutralised with sodium bicarbonate, four times a day.

Mandelic acid is obtained by the hydrolysis of the mandelonitrile produced by the action of sodium cyanide on the sodium bisulphite addition-compound of benzaldehyde. It occurs as white crystals or as a white, crystalline, odourless powder. M.p.  $118^\circ$  to  $120^\circ$ . On exposure to light mandelic acid gradually darkens and decomposes.

**Soluble** 1 in about 7 of water; freely soluble in alcohol and ether.

**Contraindications.** Mandelic acid should not be given when there is impairment of renal function.

**Uses.** Introduced to replace the ketogenic diet (*see Vol. II*) in the treatment of urinary infections. The bacteriostatic substance in urine of patients on ketogenic diet is  $\beta$ -hydroxybutyric acid. If the acid is given orally it has been found to be almost completely oxidised in the body. Mandelic acid was selected, after trial of other hydroxy acids, as being least toxic, most effective, and at the same time easily obtained. Its bacteriostatic action is only exerted when the urine is not less acid than pH 5.5, and the acidity of the urine is maintained by the simultaneous administration of ammonium chloride. During treatment the urinary pH must be controlled by tests with methyl red (the colour produced should be reddish-orange but not yellow; the test is best carried out on the early morning urine).

The original technique of administration was as follows (*Rosenheim's Routine*): 12 g. of mandelic acid is given daily in divided doses, the fluid intake being limited to 2 pints daily. The standard mixture contains 45 gr. (3 g.) of acid per oz. of water, just neutralised with sodium bicarbonate 24 gr. (1.6 g.), and flavoured with lemon; 1 oz. is given four times a day; 8 cachets, each containing 15 gr. (1 g.) of ammonium chloride, are given during the day.

The acid is now usually administered in the form of its ammonium, calcium or sodium salt. More recently it has been to some extent superseded by sulphanilamide especially in the treatment of the *B. proteus* type of urinary infection.

The effect of mandelic acid on bacteria in the urine depends upon the nature of the infecting organisms, the concentration of mandelic acid and the acidity of the urine. As the acidity of the urine increases, the concentration of mandelic acid required decreases. *Escherichia coli* is killed by 0.25% of mandelic acid at pH 5, but requires 1% at pH 5.7. *Proteus Ammoniae* is also destroyed by 1% at pH 5.7, but with 0.25% a pH of 5.3 is necessary. *Aerobacter sp.* and *Pseudomonas sp.* are more resistant, requiring 0.5% at pH 5 and 1% at pH 5.3.—H. F. Helmholz and A. E. Osterberg, *Proc. Mayo Clin.*, 1936, 373.

The relative merits of mandelate and sulphonamide therapy may be summarised as follows:—Both are efficient and may be relied on to cure 70 to 80% of cases of urinary tract infection after 8 to 14 days' treatment. Mandelate is irritant to the stomach, but the toxic effects of sulphanilamide are likely to be more serious. Mandelate is more expensive. A patient whose renal function is so impaired as to interfere with concentration of mandelate and acid will be more likely to improve on sulphanilamide, which acts at a lower concentration. The presence of prostatic enlargement and infection are indications for sulphanilamide. Infections with *B. coli* and its variants, *B. lactis aerogenes*, and most streptococci, are amenable to either drug. Sulphanilamide is ineffective in enterococcal infections, but these respond well to mandelate treatment. *B. pyocyaneus* and *B. proteus* infections require sulphanilamide. Staphylococcal infections do not yield satisfactorily to mandelate, and many cases are disappointing with mixed infection, but Uleron or sulphapyridine may be substituted. In cases of may be utilised.—T. H. Crozier, *Practitioner*, i/1940, 516.

For earlier references see previous editions.

**Acigen** (*Pharmaceutical Specialities (May & Baker), Ltd., London*). Flavoured granules containing mandelic acid, sodium bicarbonate and ammonium biphosphate. *Dose*.—2 teaspoonfuls (= 3 g. of mandelic acid).

**Neoket** (*Boots, Nottingham*). Compound effervescent granules of mandelic acid. Contains in 2 teaspoonfuls (90 gr.) mandelic acid 45 gr., sodium bicarbonate 25 gr., sodium acid phosphate 30 gr., soluble saccharin  $\frac{1}{4}$  gr., flavouring oils q.s.

*Dose*.—Two teaspoonfuls in water four times daily immediately after each meal.

In some cases the optimum urinary pH can only be attained with the supplementary administration of ammonium chloride.

**Ammonii Mandelas.**  $C_6H_5 \cdot CHOH \cdot COONH_4 = 169.18$ .

*Dose*.—50 grains (3.4 g.) four times daily in aqueous solution.

Ammonium mandelate occurs in white, very hygroscopic needles. Very easily **soluble** in water and alcohol.

It has been suggested to replace sodium mandelate and ammonium chloride, the ammonium radicle being converted by the body to urea and the mandelic acid radicle serving to acidify the urine. The nausea and vomiting sometimes caused by ammonium chloride are thus avoided. Occasionally, however, ammonium chloride must also be given to obtain the necessary acidity. More rarely an excessively acid urine is obtained, and in these cases sodium bicarbonate must be given.

Ammonium mandelate found as effective as the sodium salt in the treatment of urinary infections and usually obviated the necessity of giving the unpleasant ammonium chloride.—H. E. Holling and R. Platt, *Lancet*, i/1936, 771.

The following is a much-used formula readily made in the dispensary:—Mandelic acid 36 g., strong solution of ammonia 264 m., liquid extract of liquorice 240 m., tincture of ginger 20 m., tincture of capsicum 20 m., syrup 1 oz., mucilage of ceratonia 3 oz., chloroform water to 12 oz. 1 oz. of this mixture

contains 3 g. of mandelic acid as ammonium mandelate, and, taken with an equal amount of water, is the usual adult dose. When the solution of ammonia is added to the acid in a bottle, a syrupy solution of ammonium mandelate is formed almost immediately. It is convenient to keep this solution ready as a "stock" solution, each 55 m. representing 3 g. of acid. The colloid gum, by retarding absorption in the mouth, makes the mixture less unpalatable. The concentrated "stock" solution may be put up in capsules, which are rendered insoluble by exposing them, separated bottom from cap, in a bottle overnight with a paraform tablet. The dose can be contained in four of these capsules. The capsules keep at least a week, but probably not indefinitely.—W. A. Knight, *Pharm. J.*, ii/1936, 250.

**GASTRO-INTESTINAL INFECTIONS.** Three cases of colitis and 9 of acute gastritis were treated with ammonium mandelate. Doses of 5 ml. twice daily by mouth, until consistency of the stools became normal, were used in acute cases; three times daily for a week at a time in chronic cases. The results were good and rapid, cure being achieved in 1 to 3 days.—G. Sternberg, per *Trop. dis. Bull.*, 1940, 371.

**PYELITIS.** The following mixture is recommended for the treatment of pyelitis in children; ammonium mandelate 26 gr., liquid extract of liquorice 5 m., elixir of gluside  $\frac{1}{2}$  m., water to 1 dr. This prescription can be made up with a 50% aqueous solution of ammonium mandelate, and costs very much less than any of the proprietary preparations. It is given three or four times a day, the dosage being: up to 6 months 1 dr., from 6 months to 2 years, 1 to 2½ dr.; from 2 to 5 years, 2½ to 4 dr.; from 5 to 12 years, 4 to 6 dr. The following mixture is given in addition in a total daily dose of 3 to 8 dr.: ammonium phosphate 7½ gr., liquid extract of liquorice 5 m., acid syrup 15 m., water to 1 dr. The pH of the urine should be reduced, if possible, to 5.3. If the urine is acid enough it can in most cases be rendered sterile within several days of onset of treatment. Mandelic acid therapy should be continued for at least a week after the urine has become sterile. *B. coli* is the infecting organism in most cases of pyelitis in children, and these respond well to mandelic acid therapy; *B. proteus* pyelitis does not respond to this drug.—G. H. Newns, *Med. Pr.*, ii/1936, 516; see also W. W. Payne, *Brit. med. J.*, ii/1936, 1046.

**Effervescing Mixture.** A: Mandelic acid 36 g., water to 12 oz. B: Ammonium bicarbonate 18 g., elixir of saccharin 1 dr., water to 12 oz. Two tablespoonfuls of each mixed and taken during effervescence provides the usual 3 g. dose of mandelic acid.—W. A. Knight, *Pharm. J.*, ii/1936, 408.

**Mist. Ammon. Mandelat. (N.I.F.).** Mandelic acid 45 gr., strong solution of ammonia 20 m., liquid extract of liquorice 10 m., strong tincture of ginger 2½ m., syrup 2 dr., chloroform water to  $\frac{1}{2}$  oz.

**Ammoket (Boots, Nottingham).** Elixir of ammonium mandelate containing ammonium mandelate 52 gr., elixir of saccharin 5 m., liquid extract of liquorice 5 m., sucrose 110 gr., spirit of chloroform 7½ m., essential oils q.s., water to  $\frac{1}{2}$  oz.

**Keturex (Evans, Sons, Lescher & Webb, Liverpool).** Elixir of ammonium mandelate containing the equivalent of 45 gr. of mandelic acid per tablespoonful.

**Mandelix (British Drug Houses, London).** Elixir of ammonium mandelate containing the equivalent of 45 gr. (3 g.) of mandelic acid in 2 dr. Complete outfits are available containing the elixir, cachets of ammonium chloride and a testing outfit for determining the urinary pH.

**Mist. Ammon. Mandelat. Co. (Martindale, London)** is a lemon-flavoured preparation containing ammonium mandelate equivalent to 45 gr. of mandelic acid and 25 gr. of sodium acid phosphate in  $\frac{1}{2}$  oz.

**Calcii Mandelas.**  $(C_6H_5 \cdot CHOH \cdot COO)_2Ca = 342.35$ .

**Dose.**—50 grains (3.4 g.) four times daily in water.

A white crystalline, odourless powder with a slightly saline taste, prepared by double decomposition between sodium mandelate and a calcium salt.

Very slightly **soluble** in water; insoluble in alcohol 90%.

Unlike the sodium and ammonium salts, the calcium salt of mandelic acid is quite tasteless and does not give rise to dyspepsia. Treatment of 8 patients with urinary infections with calcium mandelate gave the same good results as

treatment with other preparations of mandelic acid.—E. Schnor, *Lancet*, i/1937 1104.

Calcium mandelate is recommended because the acidity produced is equivalent to that produced by ammonium mandelate, coupled with comparative palatability and non-production of nausea or gastric symptoms. It is, however, hydrophobic; overcome by damping with ethyl alcohol prior to suspending.—W. A. Woodard, *Pharm. J.*, i/1938, 436.

Further methods for rendering miscible with water: (i) granulate with syrup; (ii) add sodium tauroglycocholate ( $\frac{1}{2}$  to 1%); cover bitterness with a suitable agent.—W. A. Woodard, *Pharm. J.*, i/1938, 530.

**Pulvis Calcii Mandelatis (I.H.).** Calcium mandelate 50 gr., cocoa 5 gr., sugar to 75 gr. Prepare as granules. For a child of 1 year.

**Calcium Mandelate Compound (Burroughs Wellcome, London).** A flavoured powder, readily miscible with water, containing calcium mandelate equivalent to 3 g. of mandelic acid in 4.4 g. (one measureful). *Dose*.—One measureful, suspended in 4 tablespoonfuls of water four times a day. An additional acidifying substance, e.g., ammonium chloride, may be administered if required.

**Camdelate (Abbott Laboratories, London).** Calcium mandelate tablets containing 8.45 gr. (representing  $7\frac{1}{2}$  gr. of mandelic acid).

**Mandecal (British Drug Houses, London).** A flavoured powder containing 75% of calcium mandelate, readily miscible with water. For the treatment of urinary infections, the compound being decomposed by gastric juices with liberation of mandelic acid which itself renders the urine acid. *Dose*.—One level dessertspoonful (4.5 g. equivalent to 3 g. of acid) stirred in 2 fl. oz. of water, four times a day.

**Sodii Mandelas.**  $C_6H_5\cdot CHOH\cdot COONa = 174.13$ .

*Dose*.—50 grains (3.4 g.) four times daily, with supplementary treatment as with mandelic acid.

In white crystals with a faintly aromatic odour.

**Soluble** 1 in about  $1\frac{1}{2}$  of water; almost insoluble in cold alcohol 90%.

Successful clinical results with sodium mandelate given in a mixture containing sodium mandelate 50 gr., syrup of orange 1 dr., water to 1 oz. To be taken 4 times a day in water, each dose to be preceded by the requisite dose of a mixture containing ammonium chloride 30 gr., liquid extract of liquorice 15 m., water to 1 oz. The dose of ammonium chloride must be adjusted to give a urinary pH of 5.3 or less (pink with methyl red). No deleterious effects in nephritis or nephrosis.—H. E. Holling and R. Platt, *Lancet*, i/1936, 769.

The administration of sodium and ammonium mandelates is contraindicated:—(1) In the presence of raised blood urea due to renal failure, since the acidifying salts have a cumulative effect; (2) in acute febrile urinary infections; (3) in infections due to organisms capable of splitting urea and thus maintaining a constantly alkaline urine.—M. L. Rosenheim, *Brit. med. J.*, ii/1936, 1045.

By oral administration of sodium mandelate, concentrations of the acid varying from 0.25 to 1% can be obtained readily in the urine. In this range of concentration the acid will act bactericidally on most organisms at a pH ranging from 5.0 to 5.7.—H. F. Helmholz and A. E. Osterberg, *J. Amer. med. Ass.*, ii/1936, 1794.

## ACIDUM NITRICUM

B.P.

$HNO_3 = 63.02$ .

[P2] “Nitric acid.”

[S3] “Nitric acid—in substances containing less than 9%, weight in weight, of nitric acid ( $HNO_3$ ).”

*Dose*.—1 to 4 minims (0.06 to 0.25 ml.).

*B.P.* has sp. gr. about 1.42, contains 70% *w/w* of  $\text{HNO}_3$ . *U.S.P. XI*, 67 to 70%; *P. Helv. V*, 64 to 66%; *P. Ned. V*, 50%; *P.G. VI* and *P. Jap. V*, 25%; *F. E. VIII*, 63.64%; *P. Belg. IV*, 63.02%; *Fr. Cx.*, 63.05%; *P. Ital. V*, 65.3%; *P. Dan.*, 22 to 25%.

A colourless liquid emitting corrosive fumes. It forms a constant-boiling mixture with water at 120.5°, containing 68%  $\text{HNO}_3$ .

**Antidotes.** Treat as for poisoning by glacial acetic acid, *see* p. 7. Chloroform in 5-drop doses every 10 minutes will prevent the convulsions following the inhalation of nitrous fumes, as in the accidental breaking of a bottle of nitric acid.

**Uses.** A caustic for warts and condylomata.

[P2] **Acidum Nitricum Dilutum** (*B.P.C.*, *F. E. VIII*).

*Dose.*—5 to 20 minims (0.3 to 1.2 ml.).

Contains 10% *w/w* of  $\text{HNO}_3$ . *P. Belg. IV* has 12.6%.

Tonic and biliary stimulant.

**Incompatible** with alkalis, sulphides, thiosulphates, ferrous salts, and alcohol.

[P2] **Acidum Nitricum Fumans.** Sp. gr. 1.5. (*P. Jap. 1.48*; *P. G. VI* has 36%, sp. gr. at least 1.476; *P. Dan.* has sp. gr. 1.48 to 1.5.)

A reddish-brown liquid, giving off yellowish-red fumes. Used as a caustic.

[P2] **Aqua Regia** is nitric acid 3, hydrochloric acid 4.

[P2] **Acidum Nitro-Hydrochloricum Dilutum** (*B.P.C.*).

*Dose.*—5 to 20 minims (0.3 to 1.2 ml.).

Contains nitric acid, hydrochloric acid and their reaction products equivalent to about 12.5% *w/w* of nitric acid and about 13.5% *w/w* of hydrochloric acid.

**Balneum Acidum** (*B.P.C.*). Contains 15 oz. of dilute nitro-hydrochloric acid per 30 gallons.

**Potassii Nitras** (*B.P.*, *U.S.P. XI*, *Fr. Cx.*, *P. Helv. V*, *P. Dan.*).  
*Syn.* NITRE, SALTPETRE.  $\text{KNO}_3 = 101.1$ .

*Dose.*—5 to 15 grains (0.3 to 1 g.). Should be given well diluted. *U.S.P. XI* average dose 5 grains.

A white odourless crystalline powder; taste, cool and saline.

**Soluble** 1 in 4 of cold water, 1 in 0.4 of boiling water, 1 in 300 of alcohol 90%.

**Antidotes.** Empty stomach by emetic or stomach tube. Keep patient lying down and warm. Demulcent drinks freely. Stimulants, *e.g.*, brandy,  $\frac{1}{2}$  oz. in water, or hot coffee by mouth or by rectum.

**Uses.** Diuretic, to be given in dilute solution with caution. Its chief use is in the preparation of powders for burning in asthma. It has been found of value in chronic pericarditis in conjunction with other diuretics, and also in pneumonia.

Diuresis from potassium nitrate may be initiated more slowly and be of longer duration than that of other diuretics but it is less likely to cause untoward effects. It does not increase urinary acidity. It is best used in the form of enteric-coated pills of 0.5 g., of which 16 to 24 are given daily after meals. Patients are put on a salt-free, low-fluid diet and usually 50 g. of protein daily, unless the serum protein is low, when it is increased to 75 or 100 g. daily.—N. M. Keith and M. W. Binger, *J. Amer. med. Ass.*, ii/1935, 1584.

Potassium nitrate in moderate dosage can be given for long periods of time without injury. A thirteen year old boy, weighing 110 pounds (49.9 kg.), with

glomerulonephritis took 6 g. a day for a whole year, and thereby his œdema was kept under control. Intermittent administration is, however, to be preferred.—S. Amberg, *Proc. Mayo Clin.*, 1935, 739.

MÉNIÈRE'S SYNDROME. Many patients improved with potassium nitrate in a dosage of 9 g. daily, taken for three days and discontinued for two days, in conjunction with a low sodium diet.—M. N. Walsh and A. W. Adson, *J. Amer. med. Ass.*, i/1940, 130.

**Charta Nitrata** (*B.P.C.*, *P. Dan.*). *Syn.* NITRATED PAPER.

White blotting-paper, impregnated with 20% potassium nitrate solution and dried. To relieve asthma these are burnt and the fumes inhaled. Asthmatic pastilles are prepared in cones containing a mixture of chlorate and nitrate of potassium.

**Sodii Nitrates** (*Fr. Cx.*, *P. Helv. V*).  $\text{NaNO}_3 = 85.01$ .

*Dose.*—5 to 15 grains (0.3 to 1 g.).

Occurs as colourless, odourless crystals with a cool and saline taste.

**Soluble** 1 in 1 of water, 1 in 0.6 of boiling water and 1 in 100 of alcohol 90%.

Has saline, refrigerant and diuretic properties, but is seldom used in medicine. Crude sodium nitrate is known as Chile salt-petre and is used as an artificial manure.

**Uranii Nitrates** (*B.P.C.*). *Syn.* URANYL NITRATE, URANIC NITRATE.  $\text{UO}_2(\text{NO}_3)_2 \cdot 6\text{H}_2\text{O} = 502.2$ .

*Dose.*—1 to 5 grains (0.06 to 0.3 g.). Lemon yellow radioactive crystals with bitter styptic taste, efflorescent in dry air.

**Soluble** 2 in 1 of water, also in alcohol and ether. Has been used in diabetes and cancer, but is without evidence of value.

## ACIDUM OLEICUM

*B.P.*, *U.S.P. XI*, *P. Jap.*, *P. Helv. V*.

$\text{CH}_3(\text{CH}_2)_7\text{CH} : \text{CH}(\text{CH}_2)_7\text{COOH} = 282.3$ .

*Dose.*—5 to 15 minims (0.3 to 1 ml.).

A pale sherry-coloured, faintly acid, oily liquid (at ordinary temperatures) with a slight odour.

**Soluble** readily in alcohol 90%, ether, chloroform, benzene and fixed oils; insoluble in water. It dissolves most metallic oxides, thus forming indefinite solutions of oleates in an excess of oleic acid; such combinations of bismuth, copper, lead, mercury and zinc are used medicinally; they are soluble in fats. Oleic acid also dissolves alkaloids, but not their salts, *e.g.*, oleinates of aconitine, atropine, morphine and veratrine are used medicinally. Oleic acid is much more readily absorbed by the skin than oils.

Capsules of oleic acid ( $7\frac{1}{2}$  m.), one or two daily, taken in the morning on an empty stomach, have been employed in the treatment of biliary colic and to hinder the formation of gall-stones.

**Bismuthi Oleas** (*B.P.C.*).

*Dose.*—5 to 10 grains (0.3 to 0.6 g.).

A greyish-white unctuous substance or white powder containing the equivalent of 20 to 22% of  $\text{Bi}_2\text{O}_3$ , and used with zinc oxide or starch as a dusting powder in hyperæmic conditions of the skin.



**Unguentum Bismuthi Oleatis** (B.P.C.). 12½% in white soft paraffin. For chapped hands and similar conditions.

**Cupri Oleas** (B.P.C.).  $(C_{17}H_{33}COO)_2Cu = 626.46$ . (Theoretical formula for pure oleate).

Add a hot solution of copper sulphate 1 in 50 of water to a hot solution of castile soap 2.5 in 50, and wash and dry the precipitate. When cold it is in solid dark-green masses. It is an oleo-palmitate of copper, containing copper equivalent to about 12% of cupric oxide. Soluble in ether.

**Unguentum Cupri Oleatis** (B.P.C.).

Copper oleate 12½% in yellow soft paraffin. For some purposes it may be employed half strength. Ringworm is well treated with it—lightly rubbed in night and morning, also indolent ulcers, warts and corns, and it has been used to remove freckles.

**Bougies of Copper Oleate** are prepared 4 inches long containing each 5 grains (0.3 g.) of copper oleate with theobroma basis.

[P2-81] **Hydrargyrum Oleatum** (B.P.).

Yellow mercuric oxide 20% w/w, triturated with liquid paraffin and warmed with oleic acid. **Oleatum Hydrargyri** (U.S.P. XI) is made with 25% of HgO.

[P2-81] **Unguentum Hydrargyri Oleati** (B.P.). *Syn.* MERCURIC OLEATE OINTMENT.

Oleated mercury, 25%, in simple ointment.

[D-P1-81] **Oleatum Hydrargyri** (10%) *cum Morphina*.

Morphine (base) 1 is dissolved in 60 of the 10% oleate.

*Uses.* For use where the plain oleate causes pain; in syphilis in secondary and tertiary stages, excessive use to be avoided. In persistent inflammation, especially of glands and joints (such as synovitis), and in non-ulcerated syphiloderma, these oleates are more active and cleanly than mercurial ointment. They are very effective parasiticides for pediculi and ringworm.

In rheumatoid arthritis the joints thickened by fibrous adhesions and fibroid thickenings of the synovial and periarticular tissues are treated with mercuric oleate.

[P2-81] **Oleatum Hydrargyri cum Sulphure**.

Mercuric oleate 5% 4, precipitated sulphur 1, ether 3. For pediculi pubis.

[P2-81] **Unguentum Hydrargyri Oleatis Compositum**.—BROOKE'S OINTMENT.—Mercuric oleate ointment (5%) and Lassar's paste of each 41, salicylic acid 6, ichthammol 12.

In (septic) oedema of the face has been applied covered with cotton wool in thick layer and pressed down by cotton elastic bandage.

[P1-81] **Plumbi Oleas** (B.P.C.).

An unctuous granular powder obtained by interaction of solutions of lead acetate and sodium oleate.

[P1-81-83] **Emplastrum Plumbi** (B.P.). *Syn.* DIACHYLON PLASTER, DIACHYLON.

Lead plaster is a crude oleate of lead, made by the combination of olive oil (oleate and palmitate of glyceryl) and oxide of lead heated together in the presence of water. Thus made, the oleate is more adhesive than when prepared by the oleic acid solution of the oxide.

*B.P. Add. III* allows the use of arachis oil, in place of olive oil, in making lead plaster.

Is used as a "supporting" plaster in lumbago and similar conditions, and as a protective agent. Internally, it has been employed as an abortifacient.

The Inter-Departmental Committee on Abortion recommended that machine-spread plasters containing more than a defined proportion of lead oleate should be brought within the restrictions imposed upon substances in Part I of the Poisons List and the First Schedule. In some parts of the country the lead contained in machine-spread diachylon plasters is removed by scraping, and is made into pills which are sold as abortifacients.—*Report of the Inter-Departmental Committee on Abortion (H.M.S.O.)*, 1939.

**Antidotes.** Treat as for poisoning by lead compounds, see p. 855.

[P1-81-83] **Emplastrum Colophonii (B.P.).** *Syn.* EMPLASTRUM RESINÆ, ADHESIVE PLASTER.

Colophony 10, plaster of lead 85, hard soap 5. The machine-spread plaster is usually supplied with about 3 or 4 ounces of mass per yard of bleached glazed calico or brown flax holland.

**Spread Adhesive Plaster** of the Drug Tariff for *N.H.I.* purposes consists of three forms. No. 1.—A plain rubber adhesive compound spread on cotton cloth (Emplastrum Adhesivum, *B.P.C.*). No. 2.—A rubber adhesive compound containing zinc oxide spread on cotton cloth (Emplastrum Zinci Oxidi, *B.P.C.*, prepared with a flesh-coloured cloth). No. 3.—Emplastrum Colophonii, *B.P.*, spread on brown holland. When a prescription for "Adhesive Plaster" indicates a ribbon plaster, No. 1 should be supplied.

**Emplastrum Adhesivum (U.S.P. XI).**

A rubber adhesive plaster prepared with 1.5 g. of a plaster mass, consisting of rubber, resins and waxes with a filler such as zinc oxide, orris root, or starch, on 100 sq. cm. of cotton cloth.

**Taffeta Adesivo (P. Ital. V).** Dissolve fish glue 100 g. in small pieces in warm water 2000 ml., and add alcohol 95% 81½ ml. and honey 10 g. Keep warm on a water-bath and apply 4 or 5 layers to fine silk tissue (allowing each layer to dry separately). Then apply balsam of Peru 1 g. mixed with tincture of benzoin 4 g., and a final coating of glue. Dry, and keep away from air and light.

*P. Helv. V* has lead plaster 80, elemi 5, yellow beeswax 5, colophony 5, Venice turpentine (from *Larix decidua*) 5.

Local reaction to adhesive plasters occurs with considerable frequency. The following enter into the composition of adhesive plaster:—(1) Rubber, one or more of four varieties. South American Para; Plantation Smoked Sheet; Balata; Gutta siac. (2) Rosin, Grade I. (3) "Burgundy" pitch. (4) Olibanum. (5) Beeswax. (6) Zinc Oxide. (7) Anhydrous lanolin. (8) Starch. (9) Orris root. In patch tests carried out with 11 substances on 120 employees in a plaster factory, 21 showed degrees of reaction varying from slight erythema to erythema with oedema, papules and vesicle formation.—*L. Schwartz and S. M. Peck, Publ. Hlth Rep., Wash., 1935, 811.*

[P1-81] **Unguentum Plumbi Oleatis (B.P.C.).** *Syn.* UNGUENTUM DIACHYLON, HEBRA'S OINTMENT. Plaster of lead 50% and olive oil, with 1% of oil of lavender.

[P1-81] **Unguentum Diachyli Carbolisatum (Lassar)** is the same with 2% of phenol. To be rubbed in 1 to 3 times a day, or spread on linen and applied as a plaster.

These ointments are prescribed for eczema, excessive perspiration of the feet, etc.

**Zinci Oleas.**

Zinc sulphate 30 is dissolved in 60 of water, the solution is added to a solution of hard soap 90 in water 600, the mixture boiled and the zinc oleate washed, dried and powdered.

**Unguentum Zinci Oleatis (B.P.).**

Freshly-precipitated zinc oleate 1, white soft paraffin 1. Melt together and stir till cold. For some cases further dilution with soft paraffin is advisable. This ointment will cure chronic eczema.

**Zinci Oleostearas (B.P.C.).**

A white amorphous powder with faint fatty odour.

To a solution of hard soap 2, and curd soap 1 in water 15, add zinc sulphate 1 in boiling water 2; wash free from sulphate, dry and powder.

Useful for dusting on eczematous surfaces and for excessive perspiration. It may be perfumed by the addition of  $\frac{v}{100}$  of thymol, and diluted with kaolin or starch.

**Pulvis Zinci Oleostearatis Compositus (B.P.C.).** Zinc oleostearate 25, boric acid 25, starch to 100, perfumed with oil of geranium.

**Acidum Stearicum (B.P.C., U.S.P. XI, Fr. Cx., P. Jap. V, P. Dan., P. Helv. V).** *Syn.* STEARINUM (P. Austr.). *Commercial Syn.* "STEARINE," wrongly so called.  $C_{17}H_{35}COOH = 284.3$ .

This monobasic acid occurs as a hard white solid substance, and is not entirely pure. It is prepared by decomposition with superheated steam of stearin (the triglyceride of stearic acid contained with those of palmitic and oleic acids in tallow), and consists chiefly of stearic and palmitic acid. **Soluble** about 1 in 18 of alcohol 90%, readily soluble in ether and chloroform.

M.p. not below  $54^{\circ}$ . It is obtainable commercially with m.p.  $50^{\circ}$  ( $122^{\circ}F.$ ),  $52.5^{\circ}$  ( $126^{\circ}F.$ ), and  $56^{\circ}$  ( $132.8^{\circ}F.$ ). The pure acid melts at  $69.2^{\circ}$ .

**Pasta Acidi Stearici (B.P.C.).** *Syn.* UNSCENTED VANISHING CREAM.

A non-greasy preparation containing partially saponified stearic acid. Suitable for the application of substances such as quinine for the prevention of sunburn in artificial sunlight therapy.

[P1-81] **Emplastrum Hydrargyri Stearatis.**

Lead plaster 6, melt and add mercuric stearate 2, made by direct combination of mercuric oxide 10, with stearic acid 26 or *q.s.*—melt the acid and gradually stir in the oxide until all dissolved—a sand bath may be necessary. Is a substitute for mercurial plaster.

**Zinci Stearas (B.P., U.S.P. XI).**

A white powder, yielding 13 to 15.5% of  $ZnO$ . Contains a small proportion of palmitate. Manufactured by precipitating a curd soap solution with zinc sulphate.

**Insoluble** in water, alcohol and ether.

**Oleum Cocois (B.P.C., Fr. Cx.).** *Syn.* COCONUT OIL or BUTTER, OLEUM COCOS RAFFINATUM (P. Dan.). Is obtained by expression from the kernels of the coconut, the fruit of *Cocos nucifera* and *C. butyracea*. Becomes rancid on exposure to the air. Forms a readily-absorbed ointment base. Is used commercially in the preparation of "marine" soaps.

**Coconut Stearine.**—A solid fat separated from oil of coconut by cold pressure, m.p. about  $29^{\circ}$ . Has been suggested for use as a suppository basis.

**Copra** is the dried pulp of the coconut.

**Sapo Olei Cocos** (*Fr. Cx.*) is made from coconut oil 500, potassium hydroxide 125, and water 250 parts, all by weight.

**Sapo Liquidus** (*Fr. Cx.*). Coconut oil soap 450, glycerin 25, water 525 parts, all by weight.

**Liquor Saponis Olei Cocos** (*B.P.C.*). A solution of the sodium and potassium soaps of coconut oil, used as a shampoo and in dermatological practice.

**Unguentum Olei Cocos** (*B.P.C.*). 70% of coconut oil with white soft paraffin.

## ACIDUM PHOSPHORICUM

*B.P.*

$\text{H}_3\text{PO}_4 = 98.04.$

*Syn.* ACIDUM PHOSPHORICUM CONCENTRATUM; CONCENTRATED PHOSPHORIC ACID.

Contains 89% *w/w* of  $\text{H}_3\text{PO}_4$ ; sp. gr. about 1.75. This acid is considerably stronger than the concentrated phosphoric acid of the *B.P.* '14, which contained 66.3% *w/w* of  $\text{H}_3\text{PO}_4$ , the sp. gr. being 1.5. *U.S.P. XI* has 85 to 88% of  $\text{H}_3\text{PO}_4$ ; *Fr. Cx.* 49.7 to 50%, sp. gr. 1.342; *P. Ital.* 50%, sp. gr. 1.35; *P.G. VI* and *P. Ned. V* 25%.

*Dose.*—1 to 4 minims (0.06 to 0.25 ml.).

*Antidotes.* Treat as for poisoning by glacial acetic acid, *see* p. 7.

**Acidum Phosphoricum Dilutum** (*B.P., U.S.P. XI, Fr. Cx., P. Helv. V, P. Belg. IV*).

*Dose.*—5 to 20 minims (0.3 to 1.2 ml.).

Contains 10% of  $\text{H}_3\text{PO}_4$ , sp. gr. 1.054 to 1.060. *P. Dan.* has 12.2%, sp. gr. 1.067 to 1.07.

Dilute concentrated phosphoric acid (89%) 112 g. with distilled water *q.s.* to 1000 g. An acid of approximately the same strength is obtained by diluting 1 fl. oz. 170 m. of the concentrated acid with distilled water *q.s.* to 1 pint.

*Incompatible* with alkalis, ferric chloride, lime salts.

*Uses.* It has been employed as a nerve tonic, but actually it has none of the therapeutic properties of free phosphorus. Well diluted, is a pleasant cooling drink in fevers, and relieves thirst in diabetes. It renders iron preparations compatible with astringent vegetable infusions.

**Mistura Acidi Phosphorici** (*B.P.C.*).

*Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.).

Dilute phosphoric acid 15 m., with spirit of chloroform, syrup of orange and compound infusion of quassia 1 oz.

[*P*] **Mist. Phosph. c. Strych.** (*N.I.F.*).

Dilute phosphoric acid 10 m., solution of strychnine hydrochloride 4 m., concentrated infusion of quassia  $7\frac{1}{2}$  m., chloroform water to  $\frac{1}{2}$  oz.

**Calcium Magnesium Inositol-Hexaphosphorica Mitigata** (*Fr. Cx.*). A salt of the hexaphosphoric ester of inositol containing variable amounts of calcium and magnesium, and obtained from the seeds, tubers and rhizomes of various plants. It should contain not less than 19% of phosphorus.

**Ferrophytin** (*Ciba, Horsham*). Neutral colloidal iron salt of inositol hexaphosphoric acid, containing about 7.5% Fe and 6% P. Pills contain  $2\frac{1}{2}$  gr.

*Dose.*—1 or 2, 3 or 4 times a day. Also supplied in granules.

**Fortossan** (*Ciba, Horsham*). A combination of Phytin with lactose, specially suitable for infants and young children.

**Phytin** (*Ciba, Horsham*). Calcium magnesium salt of inositol hexaphosphoric acid with a phosphoric content of 22.8%. *Dose*.—One tablet 4 times daily. Neurasthenia, tuberculosis, anaemia, etc.

**Tonophosphan** (*Bayer Products, London*). Sodium salt of dimethylamino-methylphenylphosphinic acid, containing about 11% of phosphorus. Available in 1 ml. ampoules of 1 or 2% solution for subcutaneous injection and in  $\frac{1}{2}$  gr. tablets for oral administration in neurasthenia, etc. *Dose*.—1 ampoule per day or 1 tablet thrice daily.

### **Ammonii Phosphas (B.P.C.).**

*Dose*.—5 to 20 grains (0.3 to 1.2 g.).

A mixture of di-ammonium hydrogen phosphate,  $(\text{NH}_4)_2\text{HPO}_4 = 132.1$ , and ammonium dihydrogen phosphate,  $\text{NH}_4\text{H}_2\text{PO}_4 = 116.2$ , occurring in colourless crystals liberating ammonia on exposure to air. The salt now supplied usually consists of di-ammonium hydrogen phosphate.

**Soluble** 1 in 2 of water. A diuretic; increases the acidity of the urine.

**Calcii Phosphas (B.P., U.S.P. XI Supp. II).** *Syn.* CALCIUM PHOSPHORICUM TRIBASICUM (*P. Helv. V, Fr. Cx.*), "NEUTRAL" or "TRIBASIC" CALCIUM PHOSPHATE, TRI-CALCIUM PHOSPHATE, CALCIUM ORTHO-PHOSPHATE.  $\text{Ca}_3(\text{PO}_4)_2 = 310.25$ .

*Dose*.—10 to 30 grains (0.6 to 2 g.), but larger amounts (up to 75 gr.) are given as antacid.

It consists mainly of the tribasic and dibasic phosphates with some monobasic compound. The pure tribasic compound is not obtainable.

White powder made by interaction of calcium chloride with sodium phosphate and excess of ammonia at a boiling temperature. It contains about 39% of calcium and about 20% of phosphorus.

**Insoluble** in water and alcohol; soluble in dilute hydrochloric and nitric acids.

**Uses.** To supply calcium to growing bones and to assist in general nutrition. It is also given to pregnant women for the same purpose. Is a useful antacid, and has the advantage of not producing systemic alkalisation.

**GASTRIC ULCER.** Best method of avoidance of free acid and mechanical irritation is by giving hourly feeds of 5 ounces of milk, or its equivalent, through a tube, and neutralising acid by giving doses of atropine  $\frac{3}{8}$  gr. increased to tolerance: sodium citrate prevents milk clotting; manganese oxide, dose regulated to keep bowels open: and tribasic calcium or magnesium phosphate (chiefly the former) *effectually prevents acidosis*. Stomach emptied last thing at night.—A. F. Hurst, *Lancet*, i/1930, 242.

The neutral tribasic phosphates of calcium and magnesium are moderately effective antacids but are inclined to be irritating. They do not prevent alkalosis, and further experience has shown that they are not satisfactory substitutes for the other alkalis, and their use has been generally abandoned.—T. L. Hardy, *Practitioner*, i/1937, 437.

**Calcii Phosphas Di-acidus (Fr. Cx., F.E. VIII, P. Belg. IV, P. Helv. V).** *Syn.* MONOBASIC CALCIUM PHOSPHATE, ACID CALCIUM PHOSPHATE, MONO-CALCIUM PHOSPHATE.  $\text{Ca}(\text{H}_2\text{PO}_4)_2 \cdot \text{H}_2\text{O} = 252.09$ .

*Dose*.—5 to 20 grains (0.3 to 1.2 g.).

Deliquescent crystals, *insoluble* in alcohol. Contains about 16% of calcium and about 24.5% of phosphorus. It is used in the flour-milling trade and in baking.

**Calcii Phosphas Mono-acidus** (*P. Ned. V, F.E. VIII, P. Belg. IV, P. Ital. V, P. Helv. V, P. Dan.*). *Syn.* DIBASIC CALCIUM PHOSPHATE, CALCIUM MONO-HYDROGEN PHOSPHATE, DI-CALCIUM PHOSPHATE (*Fr. Cx.*).  $\text{CaHPO}_4 \cdot 2\text{H}_2\text{O} = 172.1$ .

*Dose*.—10 to 30 grains (0.6 to 2 g.). Prepared by decomposing calcium chloride with dibasic sodium phosphate.

Colourless crystalline powder with slight acid reaction, almost *insoluble* in water. Contains about 23% of calcium and about 18% of phosphorus. Used in making *Liquor Calcis Lactophosphatis*, *q.v.*

**Caldeferrum** (*Glaxo Laboratories, London*). Chocolate-coated tablets, each containing exsiccated ferrous sulphate equivalent to about 6 mg. of iron, calcium phosphate equivalent to 0.5 g. of calcium and 500 units of vitamin D. Advocated as a nutritional supplement in pregnancy and lactation and in debility and convalescence. *Dose*.—4 tablets per day.

**Calf-Rayol** (*Squibb, New York; Savory & Moore, London*). Capsules each containing dicalcium phosphate  $4\frac{1}{2}$  gr., calcium gluconate 3 gr., vitamin D 330 i.u., or tablets each equivalent to 2 capsules. Advocated for use during pregnancy, lactation, and generally where supplementary calcium is indicated. *Dose*.—1 to 2 capsules thrice daily or 2 to 6 tablets daily.

**Calfos Brand Tablets** (*Calfos Ltd., London*). Calcium phosphato-carbonate  $4\frac{1}{2}$  gr., sacch. alb. 5 gr., oil of lemon  $\frac{5}{16}$  m., excipient to 12 gr. Stated to be an assimilable and physiologically balanced form of calcium and phosphorus from natural sources. *Dose*.—1 to 2 tablets thrice daily.

**Dicalcium Phosphate Dulcet** (*Abbott Laboratories, London*). A candy preparation of dicalcium phosphate, containing 24% calcium and 20% phosphorus. Each Dulcet contains 1 g. In calcium deficiency diseases.

**Potassii Phosphas** (*B.P.C.*). *Syn.* DI-POTASSIUM HYDROGEN PHOSPHATE.  $\text{K}_2\text{HPO}_4 = 174.2$ .

*Dose*.—10 to 30 grains (0.6 to 2 g.).

A deliquescent granular powder; is given as a saline purge.

**Potassii Phosphas Acidus**. *Syn.* POTASSIUM DI-HYDROGEN PHOSPHATE, MONO-POTASSIUM PHOSPHATE.  $\text{KH}_2\text{PO}_4 = 136.1$ .

*Dose*.— $\frac{1}{4}$  to 1 drachm (1 to 4 g.).

Colourless crystals, readily soluble in water with acid reaction. Resembles the sodium compound, but is more diuretic.

**Sodii Phosphas** (*B.P., P. Ital. V, F.E. VIII, P. Jap. V*). *Syn.* DI-SODIUM HYDROGEN PHOSPHATE, MONO-ACID SODIUM PHOSPHATE (*Fr. Cx.*), TASTELESS PURGING SALT.

$\text{Na}_2\text{HPO}_4 \cdot 12\text{H}_2\text{O} = 358.2$ . *P. Ned. V, P. Belg. IV and P. Helv. V* have  $2\text{H}_2\text{O}$ . *U.S.P. XI* and *P. Dan.* have  $7\text{H}_2\text{O}$ .

*Dose*.— $\frac{1}{2}$  to 4 drachms (2 to 16 g.). *U.S.P. XI* average dose 1 drachm. Colourless crystals, efflorescent in dry air.

*Soluble* 1 in 7 of water, almost insoluble in alcohol 90%.

*Incompatible* with salts of metals and alkaloidal salts, particularly those of strychnine.

A mild aperient, well suited for a delicate stomach; small doses are antacid and diuretic; useful in bilious sick-headache and jaundice.

**Sodii Phosphas Exsicc** (U.S.P. XI, *P. Helv. V*). *Syn.* ANHYDROUS MONO-ACID SODIUM PHOSPHATE (*Fr. Cx.*).  
 $\text{Na}_2\text{HPO}_4 = 142.0$ .

*Dose.*—10 to 75 grains (0.6 to 5 g.). A white powder, readily absorbing moisture.

*Soluble* 1 in 15 of water.

**Sodii Phosphas Effervescens** (B.P.).

*Dose.*—1 to 4 drachms (4 to 16 g.).

Contains 50% of sodium phosphate. A convenient and pleasant mode of taking this useful purgative.

**Sodii Phosphas Effervescens** (U.S.P. XI).

*Average dose.*—150 grains (10 g.). Contains about 20% of exsiccated sodium phosphate with sodium bicarbonate, tartaric acid and citric acid.

**Alka-Zane** (*Warner, London*).

*Dose.*—1 teaspoonful in a glass of cold water 3 or 4 times daily after meals. An effervescing preparation of sodium, potassium, calcium and magnesium citrates, carbonates and phosphates. An antacid-diuretic, maintaining "alkali reserve."

**Calsoma** (*Abbott Laboratories, London*). Granular effervescent preparation of calcium and magnesium tribasic phosphates, for acid indigestion.

**Heptos** (*Sharp & Dohme, London*). A granular effervescent preparation containing the equivalent of 50% sodium phosphate with 3 grains of phenolphthalein and 2 grains of lithium citrate in each ounce. *Dose.*—1 to 2 teaspoonfuls as a purgative and hepatic stimulant.

**Sodii Phosphas Acidus** (B.P., U.S.P. XI).

*Syn.* SODIUM DIHYDROGEN PHOSPHATE, SODIUM BIPHOSPHATE.  
 $\text{NaH}_2\text{PO}_4 \cdot 2\text{H}_2\text{O} = 156.1$ .

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 g.). U.S.P. XI average dose 10 grains.

In colourless crystals or crystalline powder. *Soluble* about 1 in 1 of water, and 1 in 300 of alcohol 90%. Is given in alkalinity of urine with good results. Particularly useful in cystitis, and after operations on the bladder to keep the urine acid. If diarrhoea occurs, stop its use for a time. Passage of a calcium oxalate stone may be assisted by employing this salt owing to its solvent action on calcium oxalate.

**Mistura Sodii Phosphatis Acidi** (L.H.).

Sodium acid phosphate 30 gr., red mixture to  $\frac{1}{2}$  oz. (*Mistura Rubra L. H.* fuchsin 1000 grain, water  $\frac{1}{2}$  oz.).

**Mistura Sodii Acid-Phosphatis Composita** (L.H.).

With each dose of the previous mixture, patient to take hexamine 5 gr.

**Mist. Sod. Phosph. Acid.** (N.I.F.).

Sodium acid phosphate 20 gr., liquid extract of hyoscyamus 4 m., concentrated infusion of buchu 7 $\frac{1}{2}$  m., chloroform water to  $\frac{1}{2}$  oz.

**Phospho-Soda** (*Fleet*) (*C. B. Fleet Co., Lynchburg, Va.; Anglo-French Drug Co., London*). Monosodium phosphate in a non-toxic, highly concentrated aqueous solution. *Dose.*—As a laxative and liver stimulant, one teaspoonful before meals; as a purgative, 3 or 4 teaspoonfuls before breakfast; for hyperacidity due to constipation, 1 teaspoonful an hour after meals. Dilute with a third of a glass of water, and follow by a full glass.

**Recresal** (*Coates & Cooper, London*). Tablets of sodium acid phosphate. *Dose.*—2 to 5 daily. Muscular and nerve tonic.

**ACIDUM SALICYLICUM**

B.P., U.S.P. XI, P. Helv. V, Fr. Cx., etc.

Syn. *o*-HYDROXYBENZOIC ACID.**Dose.**—5 to 10 grains (0·3 to 0·6 g.).**Fr. Cx.** gives max. single dose 1 g.; max. during 24 hours 4 g.

Salicylic acid (artificial acid) of commerce is made by Kolbe's method devised in 1874, by heating sodium phenate in a current of carbon dioxide, or by a modification of it. The basic sodium salicylate so formed is decomposed with hydrochloric acid. A modification consists in heating the phenate and gas under pressure; this is more economical.

It may also be prepared from salicin and from oils of wintergreen (*Gaultheria procumbens*—Ericaceæ) and sweet birch (*Betula lenta*—Betulaceæ). This natural acid was formerly preferred for internal use.

In colourless prismatic crystals with sweetish taste. It is odourless, but its dust irritates the nostrils. M.p. 158° to 159°.

**Soluble** 1 in 500 of cold water, 1 in 3·5 of 90% alcohol, 1 in 40 of 45%, 1 in 2 of ether, about 1 in 80 of olive or almond oil, 1 in 100 of castor oil, 1 in 200 of glycerin, and 1 in 55 of chloroform; soluble also in melted fats and soft paraffin. Borax, ammonium citrate and sodium phosphate increase its solubility in water.

**Incompatibility.** Spirit of nitrous ether, quinine salts, alkalis such as sal volatile. An aqueous solution of the acid gives a deep violet colour with a trace of a ferric salt.

**Uses.** Anti-fermentative and anti-putrefactive. Internally, it is too irritating to the gastric mucosa for therapeutic use. Externally it is employed in concentrated solutions to destroy warts or corns, and in the form of a dusting powder or ointment in the treatment of skin diseases.

A solution of 1 dr. of acid in 1½ oz. of methylated spirit has been used as a paint for ringworm of nails, the applications being continued for 3 months or longer.

For scarlatinal sore throats and tonsillitis, compresses of 2% alcoholic solution have been found of value.

**Amylum Salicylatum** (B.P.C.). Salicylic acid 1, starch 9.

**Collodium Salicylicum** (B.P.C.). About 1 in 8 in acetone and acetone collodion.

[P1-S1] **Collodium Salicylicum Compositum** (B.P.C.). Syn. COLLODIUM CALLOSUM.

Salicylic acid about 1 in 8, and extract of cannabis, in acetone and acetone collodion.

**Collodium Acidum Compositum** (Fr. Cx.). Salicylic acid 2, lactic acid 2, ether 5, malachite green 0·1, in elastic collodion.

**Collodium cum Acido Salicylico** (Fr. Cx.). Salicylic acid 10%, in elastic collodion.

**Collodium Callosum** (St. B. H.). Salicylic acid 25, creosote 5, flexible collodion to 100.

**Collyrium Acidi Salicylici** (B.P.C.). 0·1% w/v.



**[P1-S1] Emplastrum Salicylicum Compositum (B.P.C.).**

Salicylic acid 20% and extract of cannabis 10% in rubber adhesive plaster. The machine-spread plaster is usually prepared with about 3½ ounces of mass per square yard of bleached cotton cloth of plain weave.

**[P1-S1] Emplastrum Salicylicum Compositum Fortius (B.P.C.).**

Salicylic acid 40% and extract of cannabis 20% in rubber adhesive plaster.

**Emplastrum Salicylicum Elasticum (B.P.C.).** 10% in rubber adhesive plaster. Plasters are also prepared with other proportions (from 5 to 40%) of salicylic acid.

WARTS often yield to prolonged maceration by a strong salicylic acid plaster—up to 60% strength—cut exactly to the pattern and outline of the lesion. The use of fuming nitric and other strong acids should be banished.—H. C. Semon, *Practitioner*, ii/1933, 479.

**Parogenum Salicylatum (B.P.C.).** *Syn.* SALICYLATED VASOLIMENT.

Salicylic acid 10% *w/v* in parogen.

**Pulvis Acidi Salicylici Compositus (B.P.C.).** *Syn.* PULVIS PRO PEDIBUS.

Salicylic acid 3% with boric acid and purified talc. For application to sweating feet.

**RINGWORM.** The most suitable powder for routine use in the prevention and treatment of mycotic infections of the glabrous skin is as follows:—Salicylic acid 5 g., menthol 2 g., camphor 8 g., boric acid 50 g., starch 35 g., applied three times daily. This is the routine treatment in the U.S. Navy; it is extremely effective and is popular with the men.—D. T. Prehn, *J. Amer. med. Ass.*, ii/1938, 685.

**Pulvis Zinci et Acidi Salicylici (B.P.C.).**

Zinc oxide 20% and salicylic acid 5% in starch.

**[P2] Salicylic Cream or Paste.**

Salicylic acid, in powder, 2, phenol 1, glycerin 10; mix.

Used as pigment when the skin is irritated by the discharge from wounds, etc., under antiseptic dressings.

**Salicylic Gauze, Lint and Wool,** each 4%.

Dissolve the salicylic acid in alcohol, *q.s.* (about 1 = 1 of dressing) and impregnate under pressure: dry.

**Unguentum Acidi Salicylici (B.P.).**

Salicylic acid, in powder, 1, white paraffin ointment 49. Useful in eczema, acne and ringworm. A 50% ointment has been used in lupus vulgaris, scabies, acute eczematous dermatitis and ringworm.

In seborrhœa, the following is useful: salicylic acid 1, precipitated sulphur 2.5, cold cream 25.

Death of a child of 7 suffering from psoriasis following application of 5% salicylic acid ointment to the psoriatic areas. Death occurred forty hours after application of the ointment.—*Per J. Amer. med. Ass.*, ii/1937, 1160.

**Adsorption through the Skin.** Salicylic acid can be transported through the epidermis into the connective tissues and thence into the blood stream. The colloids of the connective tissues retain the drug by adsorption and from these surfaces it is liberated gradually, passes into the blood and is mainly excreted

by the kidney. Adsorption may take place from soft paraffin, alcohol and water, but the first is probably the best.

[P2-81] **Mycozol** (*Parke, Davis, London*). Chloretone 5%, salicylic acid 4%, and mercury salicylate 4%, in a suitable ointment base. For the treatment of fungus infections of the skin. Also **Liquid Mycozol**, a paint containing chloretone, malachite green, salicylic acid, etc.

**Salicyl Vasogen** (previously marketed as **SALICYLOSOL**) (*Pearson, Mitcham*). A solution of salicylic acid in a partly oxygenated mineral oil. Used by massage into the skin.

### **Ammonii Salicylas** (*B.P.C., U.S.P. XI*).

$C_6H_4(OH) \cdot COONH_4 = 155.15$ . *P. Ned. V* with  $\frac{1}{2} H_2O$ .

*Dose*.—5 to 15 grains (0.3 to 1 g.); up to 30 grains (2 g.) is sometimes given. *U.S.P. XI* average dose 15 grains.

In crystalline powder, **soluble** 1 in 1 of water, 1 in  $2\frac{1}{2}$  of alcohol 90%.

**Ferri Salicylas**. *Syn.* FERRIC SALICYLATE.

*Dose*.—3 to 10 grains (0.2 to 0.6 g.).

Brownish powder of variable composition, sparingly soluble in water, but readily in solution of potassium bicarbonate. In tonsillitis, as an antiarthritic, and as a dusting powder for foul wounds.

**Mist. Ferri Salicyl.** (*N.I.F.*). Sodium salicylate 10 gr., solution of ferric chloride  $7\frac{1}{2}$  m., dilute solution of ammonia 5 m., chloroform water to  $\frac{1}{2}$  oz.

**Mistura Ferri Salicylatis** (*B.V.H.*).

Potassium bicarbonate 10 gr., sodium salicylate 10 gr., solution of ferric chloride 5 m., water to 1 oz. Useful in erysipelas and acute tonsillitis.

**Mistura Ferri Salicylata**. COHEN'S SALICYLATED IRON MIXTURE.

*Dose*.—1 to 2 drachms (4 to 8 ml.) increased.

Dissolve citric acid 14 in distilled water 200, add ammonium carbonate 6.5, then dissolve sodium salicylate 125 in this solution; add tincture of ferric chloride 125, glycerin 175, and oil of betula 4, and then add sufficient distilled water to make 1000, and filter.

### **Lithii Salicylas** (*B.P.C., Fr. Cx.*).

$C_6H_4(OH) \cdot COOLi = 144.0$ .

*Dose*.—10 to 30 grains (0.6 to 2 g.).

A deliquescent white powder, **soluble** more than 1 in 1 of water, forming a colourless, slightly acid solution, 1 in 2 of alcohol 90%, and in ether.

**Incompatible** with acids and with sodium bicarbonate.

**Used** in rheumatism and gout. Varicose veins have been treated with lithium salicylate 30%, and Tutocaine 1%. (*For references see Vol. I, 21st Edn.*)

**Effervescent Lithium Salicylate** contains 1 in 30.

*Dose*.—1 or 2 drachms.

### **Magnesii Salicylas** (*B.P.C.*).

$(C_6H_4(OH) \cdot COO)_2Mg, 4H_2O = 370.5$ .

*Dose*.—8 to 30 grains (0.5 to 2 g.).

In crystals or as a white or pinkish crystalline powder. **Soluble** 1 in 6 of water. Incompatible with acids and sodium bicarbonate.

In flatulence 15 to 45 grains thrice daily has been found useful.

**Potassii Salicylas** (*B.P.C.*).  $C_6H_4(OH) \cdot COOK = 176.1$ .

*Dose*.—10 to 30 grains (0.6 to 2 g.).

A white crystalline powder, very soluble in water.

Has given relief in rheumatic affections of the eyes.

**RHEUMATIC ENDOCARDITIS.** In some cases in which sodium salicylate gives poor results there is a good response to potassium salicylate in large doses, as shown by a fall in temperature, disappearance of intestinal disturbances, and improved general condition, with increased appetite. The treatment is preceded by four or five days' rest in bed on a diet poor in sodium and rich in potassium.—A. Tillich, *Dtsch. med. Wschr.*, 1/1937, 928.

**Sodii Salicylas** (*B.P.*, *U.S.P. XI*, *Fr. Cx.*, *P. Jap. V*, *P. Helv. V*, *P. Dan.*).  $C_6H_4(OH)COONa = 160.04$ .

**Dose.**—10 to 30 grains (0.6 to 2 g.) in a mixture or in cachets. *F.E. VIII* has max. dose in 24 hours 120 gr.

Dangerous poisoning by sodium salicylate is rare, but toxic symptoms resembling cinchonism usually appear when a total dose of 150 to 200 grains has been given.

**Intravenously** doses as large as 15 grains (1 g.) have been given, also in combination with the same amount of sodium iodide (*see Injectio Sodii Salicylatis*).

It may also be administered *per rectum* since it is rapidly absorbed by the rectal mucosa.

In white scales or shining tabular crystals with sweetish taste.

**Soluble** 1 in 1 of water, 1 in 6 of alcohol 90%, 1 in 4 of glycerin; insoluble in ether. Natural and synthetic varieties are available in commerce, the former being obtained from the natural acid. Concentrated aqueous solutions should be made with hot water and filtered; they are liable to deposit crystals of the hexahydrate on standing.

**Storage.** *P. Belg. IV* and *P. Helv. V* direct to be kept in the dark.

**DISCOLORATION OF SOLUTIONS.** Darkening of alkaline solutions of sodium salicylate may be prevented by the addition of 0.5% of sodium citrate.—A. Capellati, *per J. Amer. pharm. Ass.*, 1937, 199.

The discoloration of salicylate solutions is due to a brown oxidation product formed by the action of atmospheric oxygen. This product, "sodium salicylate-brown," the tri-sodium salt of an organic compound with the empirical formula  $C_{11}H_5O_6$ , and containing three hydroxyl groups, is an intermediate product, further oxidation giving colourless compounds.—E. A. Brecht and C. H. Rogers, *J. Amer. pharm. Ass., Sci. Edn.*, 1940, 178.

**Incompatible** with free ammonia, ammonium carbonate, and aromatic spirit of ammonia (turns brown). Gives a violet colour with iron salts. Mineral and many organic acids and acid salts cause separation of salicylic acid, *e.g.*, to dispense sodium salicylate with tincture of ferric chloride, dissolve 1 dr. of the salt in 2 oz. of water, add 30 to 40 m. of the tincture and  $1\frac{1}{2}$  oz. of a solution of potassium bicarbonate 1 dr. in 1 oz., then chloroform water to 8 oz. The result is a clear, palatable, claret-coloured mixture useful in rheumatic sore throats.

**Uses.** Sodium salicylate has a marked antipyretic and anti-rheumatic action. This combined action is employed with benefit in acute rheumatic fever, for which sodium salicylate is almost a specific. From 15 to 30 gr. is given every two hours for 3, 4 or 6 doses or until toxic symptoms, such as nausea and tinnitus, develop; then stop for 12 hours and resume with a dose of 10 to 15 gr. three times daily for several weeks. Gastric irritation is

lessened by giving at the same time an equal or double quantity of sodium bicarbonate. Children tolerate large doses well.

Sodium salicylate has also been used in chronic rheumatic diseases, but the effects are far less satisfactory than in acute rheumatic fever. Similarly, it has been used for antipyretic action in typhoid, malaria and other pyrexial diseases, but in this respect it is inferior to quinine.

It also possesses cholagogue properties, increasing the amount and fluidity of the bile, and has been employed in doses of from 5 to 10 grains four to six times daily in catarrhal jaundice and in the treatment of gall-stones.

In tonsillitis and other forms of sore throat, especially where there is a rheumatic history, doses of 10 to 15 gr. every four hours are useful, and in neuralgia, sciatica, lumbago and acute neuritis it may be given for the relief of pain.

The itching of pruritus ani may be instantly relieved by the application of a very minute quantity.

In encephalitis lethargica good results are said to have been obtained by daily intravenous injections of 15 gr. in an ounce of normal saline, increased gradually to 45 gr.

During recent years it has been widely employed as a sclerosing agent for varicose veins (*vide infra*).

The use of sodium salicylate is contraindicated in the presence of renal impairment.

**ACUTE RHEUMATISM.** Relapses found to be common when the dose was reduced too rapidly or the treatment stopped. It might be considered reasonable to keep all cases of rheumatic fever, except the most trivial, on a daily dosage of 120 gr. for a month after admission to hospital. The initial dose to be aimed at in an adult should be 200 to 240 gr. daily, with double the quantity of sodium bicarbonate, continued until toxic signs develop or the temperature has been below 99°F. for 24 hours. Thereafter a reduction to 180 to 150 gr. might be allowed for 10 days, and after that 120 gr. until the end of the fourth week, continuing with daily doses of 60 gr. until the patient is ready to be allowed out of bed, when 30 to 45 gr. of acetylsalicylic acid might be substituted for a time.—R. M. Murray-Lyon, *Edinb. med. J.*, Feb., 1936, 84.

In acute and subacute rheumatism in children, sodium salicylate intramuscularly is of advantage, 1 gr. for each year in 1 ml. water once a day for 4 days. Temperature normal in 24 hours and pains gone—but does not control rheumatic cardiac disease.—E. C. Warner, *Lancet*, ii/1930, 719.

It is possible to give a child of ten years 240 gr. of sodium salicylate every day for months, without any great difficulty or any disadvantage; indeed, the child and the carditis improve on such a dosage. But the child must be kept at rest, fed on a low protein diet, given adequate quantities of fluid, have a daily action of the bowel, and must take twice as much sodium bicarbonate—480 gr. The best way to prescribe the salicylate is in doses of 20 gr. two-hourly with 40 gr. of bicarbonate and some syrup and a flavouring agent. By these means the effects of acute rheumatic carditis can be minimised and cardiac effects rendered less severe and less common.—K. D. Wilkinson, *Practitioner*, i/1937, 378.

**Fatal Intoxication** in a child of 10 years treated for rheumatic endocarditis. After 5 days' salicylate treatment (2 g. intravenously and 5 g. rectally) symptoms of intoxication due to an acidoketosis of salicylate origin, together with renal insufficiency, developed, and despite intensive alkalisation death occurred three days later. Post-mortem revealed discrete renal lesions and massive fatty degeneration of the liver.—G. Paiseau, per *Brit. med. J. Epit.*, ii/1934, 61.

**RHEUMATIC POLYARTHRITIS** well treated by *large doses*, giving 10 times daily at 2-hourly intervals 50 ml. of a solution containing sodium salicylate 30 g., sodium bicarbonate 60 g., syrup of orange 300 g., and distilled water to 1000 ml. When fever and pains have disappeared, reduce to 4-hourly intervals. Quick

cure in acute cases, and the accompanying endocarditis is improved or cured.—J. T. Peters, *J. Amer. med. Ass.*, ii/1929, 958.

**SCIATICA.** Intravenous injections consisting of 20 ml. of an aqueous solution containing 15 gr. of sodium salicylate and 15 gr. of sodium iodide rapidly cured 20 cases of primary sciatica, but produced no permanent result in 12 cases of secondary sciatica (due to some extraneous pathological condition). The injection should be given slowly and care taken to avoid inadvertent injection into the tissues. In primary sciatica pain usually ceases within 10 minutes.—H. B. Sutton, *Lancet*, ii/1939, 1169.

### ***Sodium Salicylate as a Sclerosing Agent.***

Sodium salicylate in 20, 30 or 40% solution may be used as the sclerosing agent in the injection treatment of varicose veins, the dose being 6 to 10 ml. of the 20% at the first sitting, then 4 to 5 ml. of the 30% and finally 2 to 4 ml. of the 40%. The veins rapidly acquire a toleration for the drug if obliteration does not occur rapidly. The injection, especially of the 40% solution, may cause intense pain, commencing some seconds after injection and lasting for 2 to 3 minutes. Immediate pain on injection is an indication of extraveneous escape of the sclerosing solution. Addition of  $\frac{1}{2}$ % of procaine hydrochloride has been advised, but may prevent recognition of extravasation of the solution.

There are several disadvantages, including possible loss of time in testing sensitivity of the patient, acquirement of tolerance by veins if they are not quickly obliterated, cramp during administration, ulceration if leakage occurs, uncontrollable effect.—A. H. Douthwaite, "The Injection Treatment of Varicose Veins." H. K. Lewis, 1927.

V. Meisen recommends sodium salicylate 25% and sodium chloride 10%, which is practically painless. *Max. dose.*—10 ml. Cannula (not too sharp) is inserted with patient standing; rotate once or twice when blood flows from it to see that it has not caught in the opposite wall. The patient then lies down with leg on a special stand. When varices are empty commence injection very slowly, stopping if flow is resisted or if patient feels pain. For injections in the neighbourhood of the malleoli inject  $\frac{1}{2}$ % Novocaine direct into the varix. Massage lightly after injection. Repeat the treatment every other day and if both legs are affected treat one every day.—*Lancet*, i/1927, 1355.

The standard injection for a medium-sized vein is 5 ml. 30% solution in 10% saline, and for a large vein 7 ml. of 40% solution in 10% saline. Inject with limb emptied of blood and from below upwards. The effect can be judged after a fortnight. Local analgesics added to allay the pain found entirely negative.—G. H. Colt, *Brit. med. J.*, ii/1929, 850.

25% saline with 5% salicylate is a good average "guidable" solution for those who prefer saline to salicylate.—G. H. Colt, *Brit. med. J.*, i/1930, 760.

**VARICOSE ULCERS.** As the result of a questionnaire to 550 medical men, A. P. Luff concludes that the treatment is best limited to two procedures: (1) Injection of veins (preferably with sodium salicylate) in combination with Unna's zinc gelatin for local treatment; (2) Unna's zinc gelatin alone if injection is refused or cannot be done. Ultra-violet light treatment appears very reliable in the hands of experts. The rational method of prevention of varicose ulcers is the obliteration of varicose veins.—*Brit. med. J.*, ii/1928, 1146.

See also *Dextrose, Lithium Salicylate, Quinine-Urethane, Sodium Morrhuate, and Sodium Chloride.*

**Scleroveine** (Bengué, London). Sodium salicylate solution in ampoules for varicose vein injection.

**Effervescent Sodium Salicylate.** This is made in two strengths—5 and 10 grains in a drachm. *Dose.*—1 drachm (4 g.) or more.

**Mist. Sod. Sal. (N.I.F.).**

Sodium salicylate 10 gr., sodium bicarbonate  $12\frac{1}{2}$  gr., concentrated compound infusion of gentian 15 m., water to  $\frac{1}{2}$  oz.

**Mist. Sod. Salicyl. (P.M.H.).** Sodium salicylate 20 gr., sodium bicarbonate 20 gr., sodium thiosulphate 1 gr., peppermint water to 1.

**Mist. Sod. Sal. Co. (N.I.F.).** Sodium salicylate 10 gr., sodium bicarbonate 10 gr., potassium citrate 10 gr., concentrated compound infusion of gentian 15 m., water to  $\frac{1}{2}$  oz.

[P1] **Mistura Coryzæ (B.V.H.).**

Tincture of catechu 15 m., sodium salicylate 6 gr., ammonium chloride 5 gr., compound tincture of cinchona 1 dr., compound tincture of chloroform and morphine 5 m., syrup of tolu 30 m., syrup of lemon 30 m., glycerin 15 m., mucilage of acacia 15 m., liquid extract of nux vomica  $\frac{1}{2}$  m., water to 1 oz.

Apparently a bad example of polypharmacy but if any ingredient be omitted it disagrees with some patients. As it stands it can be taken by everybody.—A. T. Todd, *Practitioner*, 1934, 731.

**Strontii Salicylas.**  $(C_6H_4(OH) \cdot COO)_2Sr, 2H_2O = 397.9$ .

*Dose.*—5 to 20 grains (0.3 to 1.2 g.).

A white crystalline powder, slightly soluble in water and in alcohol. Used for chronic gout, and is a good intestinal antiseptic. In chronic sciatica 10 to 15 grain doses are stated to act better than other salicylates.

**Intravenously** 10 ml. of 5% solution, has proved useful in chronic affections of the joints. The lactate may be given orally, and, in severe pain, the bromide intravenously in place of the salicylate.

**Methylis Salicylas (B.P., U.S.P. XI, Fr. Cx., P. Helv. V).**  
**Syn. ARTIFICIAL (OR SYNTHETIC) OIL OF WINTERGREEN.**  
 $C_6H_4(OH) \cdot COOCH_3 = 152.1$ .

*Dose.*—5 to 15 minims (0.3 to 1 ml.). *U.S.P. XI* average dose 12 minims.

*U.S.P. XI* gives *Oleum Gaultheriæ* and *Oleum Betulæ* from the bark of *B. lenta* (Sweet Birch) as synonymous with methyl salicylate.

*P. Belg. IV* directs methyl salicylate to be given when *Essence de Wintergreen* is prescribed. *F.E. VIII*—May be either synthetic or natural. *P. Ital. V*—Synthetic only.

A colourless liquid, with wintergreen odour.

May be prepared by carefully distilling a mixture of salicylic acid 2, methyl alcohol 2 and sulphuric acid 1. **Miscible** with alcohol 90%, ether, chloroform or glacial acetic acid.

**Antidotes.** Empty stomach by emetic, or by using stomach tube with 4 oz. of sodium bicarbonate in 2 gallons of water. Give water freely, with sodium bicarbonate or magnesia, then milk and demulcent drinks. Keep patient lying down and warm.

**Poisoning** due to swallowing 1 oz. of methyl salicylate. Recovery after forcing liquids by the mouth, 2% solution of sodium bicarbonate by proctoclysis and wrapping patient with blankets.—*J. Amer. med. Ass.*, ii/1925, 306.

Less than 15 ml. *per os* has caused more than one fatality in infants. 13 cases of poisoning have been recorded, with 6 deaths.—*Brit. med. J. Epit.*, i/1928, 57.

**Uses.** Is readily absorbed when applied to the skin, and is an efficient application in lumbago, sciatica and rheumatic pain, either alone or as a paint, liniment or ointment. Also used for furunculoid ulcers, orchitis and mumps.

**Emplastrum Methylis Salicylatis.** A rubber base machine-spread plaster containing in the mass about 2% of methyl salicylate, and spread with about 4 ounces per yard on bleached cotton cloth.

**Linimentum Methylis Salicylatis (B.P.C.).**

*Syn. LINIMENTUM BETULÆ COMPOSITUM.*

Rectified oil of camphor 1 in 4, with menthol, oil of eucalyptus and methyl salicylate.

[P.] **Linimentum Methylis Salicylatis Compositum** (B.P.C.).

Rectified oil of camphor 1 in 4, with menthol, chloral hydrate, methylsalicylate and chlorophyll.

**Linimentum Methylis Salicylatis Oleosum** (B.P.C.).

Syn. **LINIMENTUM METHYLIS SALICYLATIS SIMPLEX** (N.I.F.).

Methyl salicylate 25% v/v in rape oil.

**Unguentum Methylis Salicylatis** (B.P.C.). Syn. **UNGUENTUM METHYLIS SALICYLATIS FORTE**.

Contains 50% w/w of methyl salicylate.

**Unguentum Methylis Salicylatis Dilutum** (B.P.C.).

Contains 25% of the strong ointment in hydrous wool fat ointment.

**Unguentum Methylis Salicylatis Compositum** (B.P.C.).

Syn. **UNGUENTUM METHYLIS SALICYLATIS COMPOSITUM FORTE**, **UNGUENTUM BETULÆ COMPOSITUM**, **UNGUENTUM ANALGESICUM**. **ANALGESIC BALM**.

Contains methyl salicylate 50% w/w, menthol 10% w/w, oil of cajuput and eucalyptol in a beeswax and wool fat basis.

**Unguentum Methylis Salicylatis Compositum Dilutum** (B.P.C.).

Contains 25% of the strong compound ointment in hydrous wool fat ointment.

**Analgesic Balm** (Parke, Davis, London). Menthol, methyl salicylate and lanolin. Muscular pain, rheumatism, etc.

**Balmosa** (Oppenheimer, Son & Co., London). A non-greasy, analgesic cream containing methyl salicylate and rubefaciants.

**Lodynic Unguentum Rubefaciens** (Research Products, London). Methyl salicylate 20, oil of turpentine 10, menthol 7.5, sodium ricinoleate 1 in 500, oleoresin of capsicum 2, lanolin 2 parts and beeswax 1 part to 100. As a counter-irritant in rheumatism, sciatica, etc.

**Menthofax** (Burroughs, Wellcome, London). Contains methyl salicylate 50%, menthol 10%, eucalyptol 2.5%, oil of cajuput 2.5%, white beeswax 20% and hydrous wool fat 15%.

**Mesotan** (Bayer Products, London). Methoxymethyl salicylate. Used in the form of a paint, diluted with 1 to 4 parts of olive or other oil as a counter-irritant.

**Methylsal Balm** (Martindale, London). Contains methyl salicylate 7, in combination with menthol 5%. Also prepared containing 25% and 33% of methyl salicylate (with menthol 5%). For analgesic effect in rheumatism.

**Oleum Betulæ** (B.P.C.). Syn. **OIL OF SWEET BIRCH**, **OIL OF WINTERGREEN**, **OLEUM GAULTHERIÆ**.

**Dose**.—5 to 15 minims (0.3 to 1 ml.).

Formerly obtained from *Gaultheria procumbens*, now exclusively from *Betula lenta*. Contains not less than 98% w/w of esters, calculated as methyl salicylate.

The oil has similar properties to salicylic acid. 10 to 20 minims are given every 3 or 4 hours in rheumatism and sciatica. With olive oil externally for rheumatism.

**Reipar Ampoules** (Anglo-French Drug Co., London). Natural salicylic acid in distilled *Betula lenta* water. **Dose**.—8 to 10 ml. daily subcutaneously, but not more than 1 ml. at one locality. Rheumatism, sciatica, gout, etc.

**Methylis Phthalas**. Syn. **DIETHYL PHTHALATE**.  $C_6H_4(COOC_2H_5)_2$ . A colourless, odourless, somewhat syrupy liquid with acrid taste. B.p.  $290^\circ$  to  $300^\circ$ . Insoluble in water, soluble in alcohol 90% and in oils and aromatic hydrocarbons. Used as a denaturant in surgical spirits and perfumes.

**Salicinum** (B.P., U.S.P. XI, Fr. Cx.).

$C_6H_{11}O_5 \cdot O \cdot C_6H_4 \cdot CH_2OH = 286.1$ .

**Dose**.—5 to 15 grains (0.3 to 1 g.) in cachets, tablets or in aqueous solution—the taste being covered with liquid extract of

liquorice, or small doses may be given in a pill with glycerin of tragacanth.

A glucoside in colourless shining trimetric tabular crystals, without odour, taste moderately bitter. Obtained from various species of *Salix* and *Populus* especially *S. fragilis*.

**Soluble** 1 in 28 parts of cold water, and 1 in 80 of alcohol, but insoluble in ether or chloroform.

**Uses.** Given for influenza and as a prophylactic. In rheumatic fever it acts similarly to sodium salicylate. 20-grain doses hourly, or 30 grains every 2 or 3 hours. 60 grains have been given, repeated in 2 hours without ill effect. It is given to reduce fevers, *e.g.*, of malaria or phthisis. Is of value in psoriasis when given in a dose of 10 to 15 grains three times a day. It is not adapted for use as an external antiseptic.

**Effervescent Salicin.** *Dose.*—1 drachm. Contains 5 grains in 1 drachm.

**Tabletæ Salicini** (*B.P.C.*) contain 5 gr. (0.3 g.).

**Salol** (*B.P.C.*, *P. Belg.* IV, *F.E.* VIII, *U.S.P.* XI, *P. Helv.* V). *Syn.* PHENYL SALICYLATE (*Fr. Cx.*, *P. Jap.* V).

$C_6H_4(OH) \cdot COOC_6H_5 = 214.1$ .

*Dose.*—5 to 20 grains (0.3 to 1.2 g.) in cachets, suspended in milk, or in mixtures suspended with tragacanth. *Fr. Cx.* and *P. Belg.*: *Max. single dose*, 15 gr.; *max. during 24 hours*, 90 gr. *P. Helv. V* has *max. single dose* of 30 grains.

Small crystals, with a slight wintergreen odour. *M.p.* 42° to 43.5°.

**Soluble** 1 in 15 of alcohol 90%, 1 in 10 of liquid paraffin, in fixed oils, and a trace in glycerin. Almost insoluble in water.

**Dispensing Note.** Taken internally as such it is liable to form intestinal calculi and should be triturated and prescribed with some inert powder or as an emulsion. When prescribed in an emulsion with an oil, *e.g.*, castor oil, dissolve it in the oil before proceeding. Melt the salol in the oil in a warmed mortar; emulsify with acacia, using hot water to complete."

**Uses.** Antiseptic and antipyretic. In the small intestine it splits up into its component parts, both being found in the urine which becomes very dark. It has been used as an intestinal antiseptic, but effective doses would be toxic owing to liberation of phenol. It is mainly employed as a coating for enteric pills.

**SALOL COATING OF PILLS** is conducted by employing salol melted. This renders the pill insoluble in the acid gastric juice, but soluble in the alkaline fluid of the intestine; hence suitable for purgatives to act on the bowels, and for administering antiseptics in eczema and urticaria.

**Liquor Salolis Compositus** (*B.P.C.*). *Syn.* SALOL MOUTH WASH. Salol 2.5% with thymol, oil of peppermint, oil of anise, elixir of saccharin and alcohol 90%. For use, add  $\frac{1}{2}$  to 1 teaspoonful to a tumbler of water.

**Pigmentum Salolis** (*B.P.C.*). Salol 1 in 300 in glycerin and alcohol 90%. For septic tonsils.



**Salol Catheter Oil.** Salol 1, castor oil and almond oil, of each 15. Does not dissolve the varnish of catheters.

**Salol cum Camphora.** *Syn.* SALOL CAMPHOR.

Salol 3, camphor 2, heated together, combine to form a viscid liquid, which has been used as an antiseptic in place of iodoform. Prepared with 10% only of camphor, quickly crystallises, and when powdered is suitable for application where liquid is not practicable.

Useful in suppuration of the middle ear; non-irritating.

**Tabellæ Salolis** (*B.P.C.*) contain 5 gr. (0.3 g.).

**Unguentum Salol cum Menthol.**

Salol 4, menthol 2, olive oil 4, wool fat to 100. For fissures of the skin, *e.g.*, in chapped hands.

**SUNBURN.** A 10% cream made by dissolving the salol in a minimum amount of liquid paraffin and mixing this solution with a base of cold cream, makes an effective application for the absorption of ultra-violet rays and prevention of sunburn.—*H. Sharlit, Arch. Derm. Syph., N.Y., Aug., 1935, 291.*

**Saliod** (*Gabail*) (*Anglo-French Drug Co., London*). Ampoules of 5 ml. contain 1 g. of salol and 0.1 g. of iodine, with 0.02 g. of camphor, in ether-purified olive oil. *Dose.*—5 ml. intramuscularly every 2 days. Chronic rheumatism.

**Ethylis Salicylas.**  $C_6H_4(OH) \cdot COOC_2H_5 = 166.17$ .

A colourless liquid of aromatic odour, with b.p.  $225^\circ$  to  $234^\circ$ , and properties similar to those of the methyl compound. Soluble in alcohol.

**Amylis Salicylas.**  $C_6H_4(OH) \cdot COOC_5H_{11} = 208.1$ .

Colourless liquid with carnation odour, used principally in perfumery. Has been used for painting on rheumatic joints.

**BURNS**, especially from acids, are treated with a pad soaked in it, the part being first dried and then flooded with water and neutralised with dilute ammonia.

**Borneol Salicylate.** In muscular rheumatism and acute neuralgia, by inunction or by painting over affected part. Apply  $\frac{1}{2}$  to 1 drachm with equal quantity of olive oil.

**Butylis Salicylas.**  $C_6H_4(OH) \cdot COOC_4H_9 = 194.2$ .

A colourless liquid with a powerful fragrant odour. B.p.  $267^\circ$ . It is used in perfumery.

**Salicyl Salicylate.** *Prop. Name.* DIPLOSAL (*Boehringer, Mannheim; Coates & Cooper, London*).  $OH \cdot C_6H_4 \cdot COO \cdot C_6H_4 \cdot COOH = 258.1$ .

Tablets contain  $7\frac{1}{2}$  gr. *Dose.*—1 or 2 tablets, 4 to 6 times daily.

Salol in which the phenyl group is replaced by salicylic acid. White odourless needles melting at  $147^\circ$ . Insoluble in water and dilute acids, soluble in alcohol. Used for rheumatism, neuralgia, and cystitis.

Pharmacological experiments showed that the compound remained unchanged for 6 hours in the gastric juice, but was decomposed in 2 or 3 minutes in the duodenal secretion. Hence it does not cause gastric disturbances.

**Estersil** (*Johnson & Sons, London*). Ethyl and propyl esters of salicylglycollic acid, 49% of each, with oil of lavender 2%. Liquid, for external application in rheumatism.

**Mycoceten** (*Leo, Copenhagen; Bencard, London*). Preparations (powder, spirit, ointment) containing oxybenzoic acid ester and salicylic acid. Mycotic eczema.

**Salen** (*Ciba, Horsham*). Methyl and ethyl glycollic acid esters of salicylic acid. An oily liquid readily soluble in alcohol, ether and castor oil. It is odourless and non-irritating, and is used for local application in rheumatic affections, etc. **Salenal.** An ointment containing 33 $\frac{1}{3}$ % of Salen.

**Sal-Ethyl Carbonate** (*Parke, Davis, London*). Salicylic ethyl ester carbonate in 5 gr. tablets. *Dose.*—1 to 3 tablets with water. For the relief of acute rheumatism, etc.

**Spirosal** (*Bayer Products, London*). Monoglycol salicylate. Applied externally, diluted with alcohol or olive oil, or in an ointment, as an antirheumatic.

**T.C.P.** (*British Alkaloids Ltd., London*) is stated to be a 1% aqueous solution of "trichlorophenylmethyliodosalicyl" with a R.W. coefficient of 10 calculated on the pure salt. It is a non-toxic antiseptic advocated for local application to wounds, ulcers, boils, burns, chilblains, skin affections, insect bites and stings, nasal catarrh (diluted 1 in 2 or 3 of water) and conjunctivitis (1 in 10), etc.

**T.C.P. B3 Colloidal Emulsion** contains trichlorophenylmethyliodosalicyl 1%, tribromoacetylthiodooxybenzoic acid 2%, T.C.P. bismuthate 1.5% colloidal aluminium silicate 2%, glycerin 3%, distilled water 90.5%. For the treatment of bacillary infections of the alimentary tract such as dysentery, colitis, gastro-enteritis, etc. *Dose*.— $\frac{1}{2}$  oz. in water twice a day.

**T.C.P. Ointment No. 33** contains trichlorophenylmethyliodosalicyl 15, iodine (as tincture) 0.42, methyl salicylate 4, sulphur 3.5, and colloidal kaolin 22.65 with camphor, tannic acid, salicylic acid, borax, boric acid, creosote and glycerin in a paraffin base. For eczema, hæmorrhoids, chilblains and rheumatic conditions.

**Esters of *p*-Hydroxybenzoic Acid.** Various esters of *p*-hydroxybenzoic acid, the *para* isomeride of salicylic acid, and its salts are used as preservatives in cosmetic, pharmaceutical and other preparations, especially on the Continent. They have the advantages of being tasteless, odourless, inert, stable and non-toxic substances.

Esters of *p*-hydroxybenzoic acid usually possess excellent preservative action in most cosmetic creams, but they cannot be recommended for the preparation of *sterile solutions*, or in the preservation of neutral jellies for therapeutic use, or in the formulation of antiseptic mouth washes and similar products.—R. G. Harry, *Mfg. Chem.*, 1940, 45.

**Butoben** (*Merck, Rahway, N.J.*). *n*-Butyl-*p*-hydroxybenzoate occurring as a white crystalline powder, almost insoluble in water but soluble in organic solvents.

It is non-irritant and is perfectly satisfactory in the preservation of cosmetic creams and in eye lotions.—R. G. Harry, *Mfg. Chem.*, 1940, 46.

**Nipagin M** (*Nipa Laboratories, Cardiff; P. Samuelson, London*).  $C_6H_4(OH) \cdot COOCH_3 = 152.1$ .

Nipagin M is the methyl ester of *p*-hydroxybenzoic acid, occurring as a white crystalline powder, m.p. 126° to 127°. Soluble 1 in 400 of water at room temperature if the solution is prepared by boiling; soluble in alcohol as follows: 1 in 2½ (95%), 1 in 5 (70%), 1 in 17 (50%), 1 in 143 (20%); also soluble in warm oils (1 in 40), and in glycerin (1 in 80 at 70°). It is used as a preservative in a strength of from 0.05 to 0.25% against moulds and yeasts.

Quantitative tests on methyl *p*-hydroxybenzoate confirm that it is poor in germicidal power in comparison with *p*-chlor-*m*-cresol. A 0.2% solution is not an efficient preservative for hypodermic injections; it is less germicidal than 5 p.p.m. of copper sulphate.—H. Davis, *Quart. J. Pharm.*, 1940, 32.

**Sodium-Nipagin M** is the sodium salt, soluble 1 in 5 of water. It is used in a strength of 0.1 to 0.25% as a preservative in aqueous preparations, preferably in conjunction with other related esters.

**Nipagin A.**  $C_6H_4(OH) \cdot COOC_2H_5 = 166.7$ . Ethyl *p*-hydroxybenzoate. Used for the preservation of fatty emulsions, creams, etc., in the proportions of 0.05 to 0.15%.

**Nipabenzyl** (*Nipa Laboratories, Cardiff; P. Samuelson, London*).

$C_6H_4(OH) \cdot COOCH_2 \cdot C_6H_5 = 228.2$ . Benzyl *p*-hydroxybenzoate. Soluble 1 in about 500 of water; readily soluble in oils and glycerin. It is used similarly.

**Nipasol M** (*Nipa Laboratories, Cardiff; P. Samuelson, London*).

$C_6H_4(OH) \cdot COOC_3H_7 = 180.2$ . The propyl ester of *p*-hydroxybenzoic acid. Slightly soluble in water (1 in 2000, prepared by boiling); also soluble 1 in 40 of warm oils, 1 in 143 of glycerin; soluble in alcohol as follows: 1 in 2 (95%), 1 in 2½ (70%), 1 in 6½ (50%), 1 in 700 (20%). It is used as a preservative for emulsions, oily preparations and albuminous solutions in the proportion 0.05 to

0.075%. Up to 0.5% is used for preventing the development of rancidity in oils. **Sodium-Nipasol M** is the sodium salt, readily soluble in water.

**Nipa 49** (*Nipa Laboratories, Cardiff; P. Samuelson, London*). A stable ester of *p*-hydroxybenzoic acid with anti-oxidant properties. It is stated to prevent the oxidation of ascorbic acid and oils, and the formation of peroxides in ether, etc.

## ACIDUM SULPHURICUM

*B.P., U.S.P. XI, Fr. Cx., P. Jap. V, P. Dan., P. Helv. V.*

$\text{H}_2\text{SO}_4 = 98.08.$

*Syn. OIL OF VITRIOL.*

[P2] "*Sulphuric acid.*"

[83] "*Sulphuric acid—in substances containing less than 9%, weight in weight, of sulphuric acid ( $\text{H}_2\text{SO}_4$ ); accumulators; batteries; fire extinguishers.*"

*Dose.*—1 to 2 minims (0.06 to 0.12 ml.).

A colourless, corrosive liquid of oily consistence. When diluted with water it evolves much heat. *B.P.* requires sp. gr. about 1.84, the acid containing not less than 95% *w/w* of  $\text{H}_2\text{SO}_4$ .

**Antidotes.** Treat as for poisoning by glacial acetic acid. Burns should be treated by the application of magnesium oxide or carbonate in powder form or as a thick paste. Sodium bicarbonate or chalk may also be used well diluted with water. The raw surface, if free from sepsis, may subsequently be protected by tannic acid solution or jelly.

**Uses.** Very occasionally as a caustic (mixed with sufficient charcoal to form a paste).

[P2] **Acidum Sulphuricum Fumans.** *Syn. NORDHAUSEN SULPHURIC ACID* or "**Oleum,**" sp. gr. about 1.9. Contains some sulphuric anhydride dissolved in sulphuric acid. When made by distillation of ferrous sulphate, ferric oxide or colcothar or polishing rouge remains behind.

"**C.O.V.**" and "**R.O.V.**" are impure commercial sulphuric acids, known as commercial oil of vitriol and brown oil of vitriol respectively.

[P2] **Acidum Sulphuricum Aromaticum (B.P.C.).**

*Syn. ELIXIR OF VITRIOL.*

*Dose.*—5 to 20 minims (0.3 to 1.2 ml.).

Contains the equivalent of about 13% *w/w* of free and combined sulphuric acid with tincture of ginger, spirit of chloroform and alcohol 90%.

[P2] **Acidum Sulfuricum Aromaticum (U.S.P. XI).**

*Average dose.*—8 minims (0.5 ml.).

Contains about 20% of free and combined sulphuric acid with fluid extract of ginger, oil of cinnamon and 80 to 85% by volume of alcohol.

**Spiritus Sulfuricus (Fr. Cx.).** *Syn. EAU DE RABEL.* Prepared by macerating red poppy petals 4 g., with a mixture of 95% alcohol 300 g., and sulphuric acid 100 g., for 4 days.

[P2] **Acidum Sulphuricum Dilutum (B.P.).**

*Dose.*—5 to 60 minims (0.3 to 4 ml.); *U.S.P. average dose* 15 minims. When given internally it is best administered through a glass tube to avoid injury to the teeth.

Is prepared by diluting 104 g. of the strong acid with water to 1000 g. An acid of approximately the same strength is obtained by diluting 1 oz. 100 m. with water to 1 pint.

Contains 10% *w/w* of  $H_2SO_4$  and has sp. gr. 1.064 to 1.073; *U.S.P. XI*, *Fr. Cx.*, *F. Norsk.*, *F.E. VIII*, *P. Jap. V* and *P. Helv. V* are similar; *P. Ned. V* is 4N., *i.e.*, 19.6%; *P.G. VI* 15.6 to 16.3%, *P. Ital. V* approx. 19%; *P. Belg.* approx. 9.8%; *P. Dan.* 9.2%.

**Incompatible** with alkalis and carbonates. It precipitates barium and calcium from solutions of their salts, also soluble lead and silver salts.

**Uses.** Similar to those of other mineral acids. Antiseptic and astringent in diarrhoea. In cholera epidemics "sulphuric acid lemonade," containing 5 to 10 m. of dilute acid per pint of sweetened water, has been taken as preventive; it is also taken by lead workers as preventive of plumbism. Dilute sulphuric acid in 20 to 30 m. doses, well diluted, every 4 hours is of value in carbuncles, boils and staphylococcal infections.

**Linctus Acidus** (*B.P.C.*).

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Oxymel 1 in 3 with dilute sulphuric acid, emulsion of chloroform and treacle.

[P1] **Mistura Acidi Sulphurici cum Opio** (*B.P.C.*).

*Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.).

Contains dilute sulphuric acid 20 m. and tincture of opium 7 $\frac{1}{2}$  m. with tincture of capsicum and camphor water to 1 oz.

[P1] **Mist. Acid. Sulph. c. Opio** (*P.M.H.*). Dilute sulphuric acid 15 m., tincture of opium 20 m., strong tincture of ginger 5 m., water to 1 oz.

**Ammonii Sulphas.**  $(NH_4)_2SO_4 = 132.1$ .

Colourless crystals soluble about 3 in 4 of water. It is made by distilling gas liquor with lime into sulphuric acid and is a source of ammonia for refrigeration and similar purposes. Its chief use is as a fertiliser and for fire proofing. It is also used for precipitating proteins from solution.

**Potassii Sulphas** (*B.P.C.*, *Fr. Cx.*, *P. Jap. V*, *P. Helv. V* *P. Dan.*).

*Syn.* SAL POLYCHRESTUM.  $K_2SO_4 = 174.3$ .

*Dose.*—15 to 45 grains (1 to 3 g.).

Colourless crystals with saline, slightly bitter taste. **Soluble** 1 in 10 of water. A saline purgative.

0.25 to 0.5% added to local anæsthetics, whether by spinal injection or peripheral blocking of nerves, enhances anæsthesia.

**Sodii Sulphas** (*B.P.*, *U.S.P. XI*, *Fr. Cx.*, *P. Jap. V*, *P. Dan.*).

*Syn.* GLAUBER'S SALT.  $Na_2SO_4 \cdot 10H_2O = 322.2$ .

*Dose.*— $\frac{1}{2}$  to 4 drachms (2 to 16 g.). *U.S.P. XI* average dose 4 drachms.

The form known as "feathery crystals" is handy for dispensing.

**Soluble** about 1 in 3 of water, also in glycerin; insoluble in alcohol.

**Uses.** Sodium sulphate is a powerful purgative, producing a copious watery evacuation without griping. Large doses are of value for removing fluid from the tissues in dropsy or ascites. Two-hourly doses of 120 grains are excellent for bacillary dysentery, and in infantile diarrhoea small doses (from 6 to 10 grains in dill water) have been advised. Externally the use of compresses

of a saturated solution of sodium sulphate is said to reduce œdema and pain in infected wounds.

**WOUNDS.** Plain lint soaked in a 12% solution of sodium sulphate and applied to the surface of any ordinary, fairly open septic wound is astonishingly effective and is preferable to the use of antiseptics. The lint is covered with oiled silk or elastic adhesive plaster and bandaged. The lint must be kept soaked with the solution and changed twice a day or more often if necessary. One of the first and almost immediate symptoms is the relief of pain.—J. C. Lyth, *Brit. med. J.*, ii/1935, 905.

Recovery of every one of 1096 infected wounds of all types by the sole use of soaks of a saturated solution of sodium sulphate. Septic œdema disappears with startling rapidity when hypertonic solution of sodium sulphate is applied at the point of entry of infection. For the purpose of hypertonic saline dressings sodium sulphate is much more effective than either magnesium sulphate or sodium chloride.—J. C. Lyth, *Lancet*, i/1940, 216; see also *Brit. med. J.*, ii/1940, 53.

Lyth's findings confirmed, but, by the addition of 0.1% acriflavine to the 10% sodium sulphate solution, spreading infections are promptly localised, sloughs separate more rapidly, and granulation and epithelization are stimulated to a far greater extent than by sodium sulphate alone.—C. J. Cellan-Jones, *Brit. med. J.*, ii/1940, 152.

**Mist. Sod. et Mag. Sulph. (N.I.F.).** Sodium sulphate 30 gr., magnesium sulphate 15 gr., syrup of ginger 20 m., water  $\frac{1}{2}$  oz.

### **Sodii Sulphas Effervescens (B.P.).**

**Dose.**—1 to 4 drachms (4 to 16 g.).

Contains 50% of sodium sulphate.

A teaspoonful or more in half a tumbler of water, taken half an hour before breakfast, is an efficient evacuant.

### **Sodii Sulphas Exsiccatus (B.P.C., Fr. Cx., P. Helv. V).**

$\text{Na}_2\text{SO}_4 = 142.1$ .

**Dose.**— $\frac{1}{4}$  to 2 drachms (1 to 8 g.).

A white powder readily absorbing moisture. On drying, crystalline sodium sulphate loses about half its weight.

**Soluble** 1 in 8 of water.

The Committee on General Chemistry of the Pharmacopœia Commission (*Report* 14) have recommended the inclusion in the B.P. of exsiccated sodium sulphate (*syn.* ANHYDROUS SODIUM SULPHATE, EXSICCATED GLAUBER'S SALT) prepared by drying sodium sulphate at 100° to constant weight.

### **Sal Carolinum Factitium (B.P.C.). Syn. ARTIFICIAL CARLSBAD SALT.**

**Dose.**—1 to 2 drachms (4 to 8 g.).

A crystallised preparation containing sodium sulphate about 55% with potassium sulphate, sodium chloride and sodium carbonate.  $1\frac{1}{2}$  drachms is approximately equivalent to 1 pint of the natural water.

**Sal Carolinum Factitium (P.G. VI, P. Ned. V, P. Belg. IV, P. Jap. V).**

**Dose.**—20 to 60 grains (1.3 to 4 g.).

A powdered preparation containing exsiccated sodium sulphate 22, potassium sulphate 1, sodium chloride 9, sodium bicarbonate 18. 53 gr. is approximately equivalent to 1 pint of the natural water.

### **Sal Carolinum Factitium Effervescens (B.P.C.).**

**Syn. EFFERVESCENT CARLSBAD POWDER.**

**Dose.**—1 to 2 drachms (4 to 8 g.).

Contains about 10% of exsiccated sodium sulphate and 40% of sodium potassium tartrate.

**Marienbad salt** is similar to powdered artificial Carlsbad salt. **Marienbad salt tablets** may be prepared containing 60 grains of the mixture.

**Marienbad Antiobesity Tablets.** *Dose.*—One or two at bedtime. Aloes  $\frac{1}{2}$  gr., rhubarb 1 gr., cascara extract  $\frac{1}{2}$  gr., Marienbad salt  $\frac{1}{2}$  gr., fucus extract  $\frac{1}{2}$  gr.—*Pharm. J. Formulary.*

**Sal Emsanum Facticium** (*P. Ned. V*). Exsiccated sodium sulphate 10, potassium sulphate 10, sodium chloride 265, sodium bicarbonate 715.

**Sal Hunyadi Janos Facticium** (*P. Ned. IV*). Magnesium sulphate 950 exsiccated to 500, sodium chloride 50, exsiccated sodium sulphate 450.

**Sal Vichy Facticium** (*P. Ned. V; P. Helv. V*). Sodium phosphate (cryst.) 20, potassium sulphate 50, sodium chloride 80, sodium bicarbonate 850.

**Sal Wildungense Facticium** (*P. Ned. V*). Potassium sulphate 5, calcium carbonate 190, magnesium carbonate 190, sodium chloride 240, sodium bicarbonate 375. To make artificial Wildungen water use 4.6 g. per litre.

*Dose* of each.—20 to 60 grains (1.3 to 4 g.), increased as required.

**Sodii Sulphas Acidus**, *syn.* **SODIUM BISULPHATE**,  $\text{NaHSO}_4 \cdot \text{H}_2\text{O}$ , occurs in crystals or fused masses. Is used for preparing effervescing baths.

**Nauheim Bath Salts** are prepared with this salt and sodium bicarbonate. The Nauheim water contains in addition sodium and calcium chlorides.

**Ammonii Persulphas** (*B.P.C.*).  $(\text{NH}_4)_2\text{S}_2\text{O}_8 = 228.2$ .

White crystals obtained by the electrolysis of ammonium sulphate solution. Soluble 1 in 2 of water. Is used in the preparation of the persulphates.

**Potassii Persulphas** (*B.P.C.*).  $\text{K}_2\text{S}_2\text{O}_8 = 270.3$ .

White crystals soluble 1 in 3 of water. A bleaching agent; used also in photography as a reducer. Its use as a flour "improver" is liable to cause "baker's itch."

**Sodii Persulphas**.  $\text{Na}_2\text{S}_2\text{O}_8 = 238.1$ .

*Dose.*—1 to 3 grains in water before meals.

In small white granular crystals, soluble in water. Has been recommended as an aperitive stimulant to digestion and is said to bring about an improvement in nutrition and gain in weight. It should not be used continuously for more than 3 weeks. It is best given in water in a single daily dose of 3 grains. It is a strong oxidising and bleaching agent. Liberates about 13% active oxygen. If it is desired to avoid production of free sulphuric acid, the persulphate may be mixed with  $\frac{1}{2}$  times its weight of sodium carbonate. 3 to 10% solutions as gargle and dressing. Suitable for wounds requiring moist dressing and where disinfection necessary. For small ulcers may be used as dusting powder, with equal quantity of powdered talc.

## ACIDUM SULPHUROSUM

*B.P.C.*

$\text{H}_2\text{SO}_3 = 82.08$ ;  $\text{SO}_2 = 64.06$ .

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

A colourless liquid, with strong sulphurous odour, and containing 5% of  $\text{SO}_2$ . Sp. gr. about 1.025.

**Preparation.** By roasting sulphur or by heating copper and sulphuric acid, or carbon and sulphuric acid, and dissolving the gas in water. Sulphur dioxide is also available compressed in cylinders.

**Antidotes.** Keep patient warm; mustard plaster on chest. Give narcotics if necessary. Artificial respiration.

**Uses.** This solution of sulphurous acid is applied externally as a lotion—one part to two or more of water and sometimes a

little glycerin added for affections such as chloasma, ringworm, pruritus, thrush and chapped hands, with very good results. It is sprayed into the throat for tonsillitis, diphtheria (better diluted) and asthma, or used as an inhalation, a teaspoonful to a pint of cold water. It is strongly antiseptic, and has been used in whooping cough by fumigating the room. Also diluted, for fœtor of the teeth, *e.g.* in syphilis.

Internally it has been used in cholera (freely diluted). As a rectal injection, a 1 or 2% solution of the gas. Also for gastric fermentation accompanied by *sarcinæ*, and in typhoid (20 to 30 minim doses, diluted) every 2 or 3 hours.

**Lotio Acidi Sulphurosi (B.P.C.).**

Sulphurous acid and glycerin of tannic acid, of each 1 in 4 in distilled water. Useful as a paint or spray in tonsillitis and septic sore throat.

**Magnesii Thiosulphas.** *Syn.* MAGNESII HYPOSULPHIS.

$\text{MgS}_2\text{O}_3 \cdot 6\text{H}_2\text{O} = 244.5$ .

**Dose.**—8 to 15 grains (0.5 to 1 g.) orally, or by intramuscular injection of a 10% solution.

Colourless crystals **soluble** 1 in  $1\frac{1}{2}$  of water. Used in the treatment of allergic diseases.

Spasmodic coryza and asthma, resistant cases successfully treated by magnesium thiosulphate tablets 0.5 g., 4 to 6 daily, or the intramuscular injection every fourth day for 2 weeks of 10 ml. of a 10% solution. Injections stated to be painless and amelioration of symptoms to follow almost immediately.—G. Boissel, *Pr. med.*, May 17, 1930.

Asthma of 2 to 25 years' standing treated *per os*. Results satisfactory, no contraindications.—M. J. Fenton, *Brit. med. J.*, ii/1930, 940.

**Potassii Metabisulphis.**  $\text{K}_2\text{S}_2\text{O}_5 = 222.3$ . *Syn.* POTASSIUM PYROSULPHITE, POTASSIUM BISULPHITE.

Prepared by saturating a solution of potassium carbonate or caustic potash with sulphur dioxide.

It is used as a reducing agent in photography and, in small quantities, to preserve the colour of ointments containing resorcinol. Also used in the *Campden Process* for preserving fruit, which consists of bottling the fruit in a cold solution of potassium metabisulphite and sealing the containers. The covers must be non-metallic, and cork bungs sealed with wax are recommended. The fruit will keep indefinitely when stored in this manner, and even when unsealed, provided the solution still covers the fruit, will remain good for a week or two. The fruit is boiled before use to remove the preservative. The process can be used for most soft fruits, but is of no use for vegetables.

**Sodii Sulphis (B.P.C.).**  $\text{Na}_2\text{SO}_3 \cdot 7\text{H}_2\text{O} = 252.2$ .

**Dose.**—5 to 20 grains (0.3 to 1.2 g.).

Colourless efflorescent crystals slowly oxidising in air to sulphate (keep in stoppered bottles).

**Soluble** 1 in 2 of water, 1 in 25 of glycerin; slightly in alcohol 90%. Incompatible with acids.

**Uses.** Antiseptic and antizymotic. Has been used internally for fermentative dyspepsia and for *sarcinæ* in the stomach. In dilatation of the stomach, sodium sulphite in 5 to 10 gr. doses, with sodium bicarbonate and *nux vomica* between meals, is said to be of value.

Externally it is employed as a lotion in parasitic skin diseases and a 1 in 8 solution is a useful mouth-wash in stomatitis.

**Sodii Sulphis Exsiccatus.** *Syn.* NEUTRAL SODIUM SULPHITE (*Fr. Cx.*).  $\text{Na}_2\text{SO}_3 = 126.1$ .

A white powder, **soluble** 1 in 3.2 of water; slightly soluble in alcohol. It is used in photography. Being a dry powder it is convenient for transit.

**Sodii Metabisulphis.** *Syn.* SODIUM PYROSULPHITE, SODIUM BISULPHITE.  $\text{Na}_2\text{S}_2\text{O}_5 = 190.1$ .

Made by passing sulphur dioxide into a hot concentrated aqueous solution of sodium sulphite, or sodium hydroxide.

Prismatic crystals or white powder readily **soluble** in water.

The true bisulphite or acid sulphite,  $\text{NaHSO}_3$ , does not exist as a solid.

**Uses.** Antiseptic and antifermentative. Has been used as a mouth-wash in thrush and as a 10% lotion in ringworm and other skin diseases.

A solution of sodium metabisulphite 20 gr., in alcohol 90% 1 oz., peppermint oil 5 m., and glycerin 2 oz., has been used as an antiseptic throat pigment. In photographic use sodium metabisulphite is similar to the potassium salt. Is largely used as a food preservative.

**Sodii Thiosulphas** (*B.P. Add. I, U.S.P. XI, P. Helv. V, P. Jap. V, P. Dan., P. Ital. V, and F.E. VIII*). *Syn.* SODII HYPOSULPHIS (*Fr. Cx.*).  $\text{Na}_2\text{S}_2\text{O}_3 \cdot 5\text{H}_2\text{O} = 248.2$ .

**Dose.**—5 to 20 grains (0.3 to 1.2 g.), or more, *per os*. *B.P. Add. I* gives dose by subcutaneous, intramuscular or intravenous injection, 5 to 15 grains (0.3 to 1 g.). Is usually injected as a 10% solution.

Crystals **soluble** 5 in 3 of water; insoluble in alcohol.

Sterilisation of a solution of sodium thiosulphate requires special precautions, since the thiosulphate ion appears to cause a high survival-rate of bacteria. Of a number of solutions of medicaments, 12% sodium thiosulphate solution was the only one not sterilised by steaming for 30 minutes, and in tyndallisation experiments, a solution of sodium thiosulphate showed little germicidal action on spores of *B. subtilis* and *Cl. Welchii*.—H. Davis, *Quart. J. Pharm.*, 1940, 42.

**Uses.** As a lotion, 1 in 10 for chloasma, ringworm, etc. A 40% solution is employed in the treatment of scabies, followed by the subsequent application of 4% hydrochloric acid. Intravenously it is used for the prevention and treatment of stomatitis due to injections of mercury, bismuth or arsenic compounds, and also for the dermatitis sometimes caused by injections of gold compounds. For these purposes oral administration is less effective, but gold dermatitis may yield to a short course of 10 gr. doses thrice daily. Tissue reactions due to extraveneous leakage of organic arsenicals may be treated by infiltrations of a 10% sterile solution. Intravenous injection of 10 to 50 ml. of a 20% solution is of value in the treatment of cyanide poisoning.

Sodium thiosulphate is extensively employed in photography.

**ECZEMA.** 0.45 to 0.75 g. intravenously repeated daily without danger for weeks at a time.—*Lancet*, i/1931, 649.

**PELLAGRA.** Even advanced cases cured by intravenous injections of 10 ml. 10% solution, 20 to 60 injections necessary. No complications.—I. Sabry, *Lancet*, ii/1931, 1022; *J. trop. Med. (Hyg.)*, Sept., 1931, 303.



**SCABIES.** The patient takes a soap and water bath, and, after drying, a 40% aqueous solution of sodium thiosulphate is applied to the areas between the fingers, the flexural surfaces of the wrists, breasts, abdomen, buttocks, thighs and external genitalia. 15 minutes later 4% hydrochloric acid is applied in the same way, and 1 hour later the applications are repeated in the same order. The procedure is repeated the next day. On the following day the patient bathes and changes to fresh clothing. All bed linen, sleeping garments, and clothing previously used are sterilised by boiling for 5 minutes. 4 ounces of each solution is sufficient to carry out the treatment. Better results than with the Danish treatment. 10 patients out of 50 developed sulphur dermatitis.—G. V. Kulcher and W. M. Meininger, *Arch. Derm. Syph., N.Y.*, 1936, 218. Good results using 25% and 5% solutions respectively.—W. S. Parker, *Lancet*, i/1939, 987.

**Calcii Thiosulphas.**  $\text{CaS}_2\text{O}_3 \cdot 6\text{H}_2\text{O} = 260.3$ .

**Dose.**—10 grains (0.6 g.) daily.

A white, crystalline substance, efflorescing at 40°.

Readily *soluble* in water, but insoluble in alcohol.

**Uses.** Has been used internally in excessive gastro-intestinal fermentation and in skin diseases, and intravenously in arsenical or bismuth dermatitis similarly to sodium thiosulphate.

Arsenical or bismuth dermatitis treated by 0.6 g. daily intravenously of a 10% solution for 3 days and then bi-weekly injections. Exerted definite curative influence in 6 cases.—A. E. W. McLachlan, *Brit. med. J.*, i/1933, 916.

**Ametox** (*Pharmaceutical Specialities (May & Baker) Ltd., London*). Preparations of sodium thiosulphate, calcium thiosulphate or magnesium thiosulphate. The sodium thiosulphate preparation is available in ampoules of solution or of the exsiccated salt. The calcium and the magnesium preparations are in ampoules of solution, the latter also in tablets for gastric fermentation.

**Calciostab** (*Boots, Nottingham*). 10% aqueous solution of calcium thiosulphate; for the prevention and treatment of metallic poisoning from anti-syphilitic treatment. **Dose.**—6 ml. intravenously daily up to the seventh or eighth day and then every second or third day.

**Thiostab** (*Boots, Nottingham*). Sterile 10% solution of sodium thiosulphate in ampoules containing 0.3 to 0.9 g. of exsiccated salt (equivalent to 0.45 to 1.35 g. of the crystalline compound).

## ACIDUM TANNICUM

*U.S.P. XI, Fr. Cx., P. Belg. IV, P. Ital. V, P. Helv. V, etc.*

$\text{C}_{14}\text{H}_{10}\text{O}_9 = 322.1$ .

*Syn.* TANNIN.

**Dose.**—5 to 10 grains (0.3 to 0.6 g.). *U.S.P. average dose* 15 grains.

Extracted from specially fermented galls with ether containing a little alcohol and water.

**Soluble** in water 1 in 1 slowly, in glycerin 1 in 1, and in alcohol 90% 1 in 1. Almost insoluble in ether, chloroform, benzene and light petroleum. Aqueous solutions of tannic acid tend to decompose on storage.

**Incompatible** with ferric salts, acids, alkalis, silver and other metals and with gelatin. Furthermore, tannin solution precipitates the majority of alkaloids from solution, hence is occasionally employed as an antidote to these.

**Uses.** A powerful astringent but somewhat irritating. It is seldom given internally as such, since it may interfere with gastric

digestion. Externally it is valuable in overcoming tissue relaxation such as is seen in chronic inflammation of the throat and in hæmorrhoids, and its coagulant properties may be employed to arrest superficial bleeding, though it is of no value in any form of remote hæmorrhage. A 20% solution in alcohol is a useful astringent for application to spongy gums. For the tannic acid treatment of burns, employing aqueous solutions varying from 2 to 20% *vide infra*.

**ECZEMA.** For the treatment of weeping eczema it is recommended to start with a 10% solution to give quick relief, followed by a weaker solution down to 2.5%; discontinued when the weeping surface has dried; it is unnecessary to carry the treatment to the tanning stage. A bland ointment containing zinc oxide, tar, starch, and soft paraffin is then applied.—P. S. Tennant, *Canad. med. Ass. J.*, Oct., 1934, 414.

Also of value in impetigo neonatorum, the vesicles being ruptured with a swab dipped in 10% solution, followed by swabbing the areas with a 2.5% solution several times daily for 2 days.—*ibid.*

### **Tannic Acid Treatment of Burns.**

First advocated by E. C. Davidson in 1925. A 2% solution of tannic acid (originally 2½% was used) with 1-2000 of mercuric chloride is applied warm on lint wrung lightly out of the solution, the dressing being completed by covering with wool and bandaging in position. For hospital treatment the burned area should be sprayed with the solution and dried—by electric lamps in bed cases or by an electric drier—the application being repeated every hour until a thin brown layer of coagulated tissue is formed (7 to 10 applications). Tannic acid must never be used for burns of the hands or face; in the former it may produce gross crippling of the hands, and in the latter, by immobilising or deforming the eyelids, it endangers the eyes. No part of burnt area should touch bed-clothes or bed. The solution should be freshly prepared since the coagulating power decreases on keeping. Stronger solutions, *e.g.*, 5, 10 and even 20%, have been advocated, but the 2% solution is still widely employed. For burns of minor degree the application of tannic acid jelly (5%) is a valuable first-aid procedure. (*N.B.* The tannic acid treatment is now being largely replaced by the use of gentian violet jelly or spray (*see* p. 256) which produces a more supple coagulum.)

At St. Thomas's up to 1900, mortality from burns and scalds was 23 to 24% of the cases occurring annually; this was reduced to 14% with the introduction of the picric acid method, and with the introduction of the tannic acid treatment in 1928 was further reduced to 4% in 1929, 3% in 1930, 2½% in 1931, and nil in 1932 (up to October). A moderately large dose of morphine should be given at the earliest possible moment to minimise primary shock.—N. Lock, *Brit. med. J.*, i/1933, 272. *See also* P. H. Mitchiner, *ibid.*, 447, and *Lancet*, i/1933, 233.

There is no time limit after which tannic acid treatment should be abandoned and good results may be obtained by its use where sepsis is fully established. When applied to a septic surface tannic acid will form a coagulum more readily than on a surgically clean area and a crust soon dries, which, if it stays in place and can be kept hard, will supply the essential rest and protection for the inflamed tissues. Pus formation is not an indication for removal of the coagulum and incisions are seldom if ever necessary. Neither should fever be considered an indication for removal of the coagulum; in most cases it will subside in 2 or 3 days. Treatment of 18 cases of second degree cordite burns (naval men) all septic.—B. C. Murrell, *Brit. med. J.*, i/1940, 51.

A 20% solution, which produces immediate coagulation, has many practical advantages over a 2.5 or 5% solution. An antiseptic—1 in 1000 acriflavine or 1% aqueous solution of gentian violet—should be incorporated in the coagulating solution or applied immediately afterwards.—W. C. Wilson, *Practitioner*, i/1936, 398.

A 20% solution in 1-1000 acriflavine is advocated, applied by means of a camel-hair brush. The solution keeps indefinitely.—L. J. Panting, *Brit. med. J.*, i/1936, 446. The solution can also be applied as a spray.—J. A. Ross, *ibid.*, ii/1936, 312.

The application of powdered tannic acid directly to the burn has given excellent results. The serous exudate is relied upon to dissolve the powder, and the resultant scars are supple, non-cheloid and often invisible.—P. Joly and A. Vadder, per *Amer. J. Pharm.*, 1940, 231.

The following antiseptic analgesic tannic acid jelly has been prepared for use in H.M. ships:—tannic acid 20%, proflavine sulphate 0.1%, procaine 2%, in a glycerin-tragacanth base (powdered tragacanth 2%, glycerin 10%, water to 100).—J. F. Heggie and R. M. Heggie, *Lancet*, ii/1940, 391.

**The Bettman Technique.** An improvement on the usual spray of 5% tannic acid solution is to follow this by the application of 10% silver nitrate solution. Minimises shock and toxæmia and promotes more rapid healing.—A. G. Bettman, per *Prescriber*, 1935, 304.

Especially valuable in treating young children and infants with severe burns. The resulting eschar is much softer, thinner and more rubbery than that produced by tannic acid, but the most important advantage is the dramatic speed with which it is formed; it is possible even in cases of severe shock to cover the burned area immediately with dressings and clothes and to prop the child up in bed on soft pillows. The dressings do not stick, the danger of upper respiratory infections is markedly lessened and the "heat-bed" and continued spraying are not necessary. The eschar comes off in one to three weeks. The danger of argyria is discounted. The after-care of small children is most important. At least 1 litre of fluid per 10 kg. of body weight per day should be given, and in the most severe cases continuous intravenous drip is advisable.—M. B. Low, *New Engl. J. Med.*, i/1937, 553.

The weaker solutions, e.g., 2½%, have been abandoned owing to the length of time required to produce a satisfactory coagulum (an extremely important factor in infants and children) and the 20% solution has also been discarded in favour of the Bettman technique, since the eschar formed is too thick and tends to crack.—W. M. Dennison, *Lancet*, ii/1939, 1107.

The silver nitrate and tannic acid method is strongly recommended in the treatment of war burns.—S. M. Cohen, *Brit. med. J.*, ii/1940, 251.

**Collodium Stypticum (B.P.C.)** contains 15% w/v of tannic acid with benzoin and alcohol in simple collodium.

**Gargarisma Acidi Tannici (B.P.C., N.I.F.)** contains 12½% of glycerin of tannin in water.

**Pasta Acidi Tannici (B.P. Add. III).** *Syn.* TANNIC ACID JELLY.

Tannic acid 5%, powdered tragacanth 2%, chlorocresol 0.1%, alcohol (95%) 6%, in water.

The following formula has also been recommended:—Tannic acid 5 g., powdered tragacanth 2.1 g., *p*-chloro-*m*-cresol 0.1 g., potassium chloride 0.042 g., sodium chloride 1.05 g., calcium chloride 0.084 g., industrial methylated spirit 6 ml., water to 100 ml. Boil the water for 15 minutes, add the *p*-chloro-*m*-cresol, plug the flask and shake until dissolved. Cool, dissolve the tannic acid and the salts and strain through wool. Place the industrial methylated spirit in a dry wide-mouthed bottle, add the tragacanth and shake occasionally during 20 minutes. Finally add the whole of the aqueous solution to the gum-spirit suspension and shake vigorously. Store in well-closed containers in the dark.—W. A. Woodard, *Pharm. J.*, i/1938, 435.

**INFANTILE STOMATITIS.** Tannic acid jelly is a valuable treatment in infantile stomatitis (*i.e.*, those non-specific infections of the mouth in infants up to the completion of the first dentition). The mother is instructed to scrub her hands

with soap and water and then to apply a little of the jelly to the child's gums and cheeks with her finger. The soothing effect is rapid and gratifying. Applications at 2 or 3 hourly intervals are recommended.—I. Mirvish, *Lancet*, ii/1938, 1292.

**Amertan** (*Lilly, London*). A non-greasy jelly containing 5% tannic acid and Merthiolate (q.v.) 1 in 5000.

**Candatan** (*Clay & Abraham, Liverpool*). Tannic acid 10%, acriflavine 0.1% in a water-emulsifying base.

**Dettol Burn Cream No. 4** (*Reckitt & Sons, Hull*), containing tannic acid, tragacanth and Dettol, is now constantly used at the Royal Hospital for Sick Children, Glasgow, for burns of the face. Owing to its flexibility this cream is useful when the injury is situated at flexures and it is used routinely for "patching up" cracks which appear in the coagulum formed by the tannic acid and silver nitrate.—W. M. Dennison, *Lancet*, ii/1939, 1107.

**Flavotan** (*Boots, Nottingham*). Tannic acid jelly with acriflavine and amyl-m-cresol.

**Hexyltan Jelly** (*Sharpe & Dohme, London*). Jelly containing hexyl-resorcinol 1 in 2000 and tannic acid 5% in a water-soluble base.

**Tanjac** (*Evans, Sons, Lescher & Webb, Liverpool*). Tannic acid jelly with acriflavine.

**Tannafax** (*Burroughs Wellcome, London*). Tannic acid with 0.5% phenol in a water-soluble base. For burns and scalds, apply lightly, allow to dry and bandage loosely.

**Tanna-flavine Jelly** (*British Drug Houses, London*). A non-oily, water-soluble preparation containing 5% of tannic acid and a suitable proportion of acriflavine.

**Tanna-flavine Powder** (*British Drug Houses, London*). A combination of tannic acid and acriflavine in powder form issued in tubes, each containing sufficient to prepare  $\frac{1}{2}$  pint of a 2½% solution of tannic acid with a suitable quantity of acriflavine.

**Tannex** (*Allen & Hanburys, London*). Tannic acid jelly containing 5% of tannic acid and 0.1% of acriflavine in a water-soluble base.

**Tannol** (*Clay & Abraham, Liverpool*). Emulsion of acriflavine with 10% of tannic acid.

### **Glycerinum Acidi Tannici (B.P.).**

**Dose.**—10 to 30 minims (0.6 to 2 ml.).

Tannic acid 15% w/w in glycerin.

For follicular tonsillitis the B.P. glycerin of tannic acid or of alum has a most satisfactory action and causes the ejection of secretion from the follicles.—F. C. Ormerod, *Practitioner*, i/1937, 527.

### **Glyceritum Acidi Tannici (U.S.P. XI).**

Tannic acid in glycerin 1 in 5 by weight, with 1% of sodium citrate.

### [P2] **Lotio Acidi Tannici (B.P.C.).**

Tannic acid 2% w/v and mercuric chloride 1 in 2000 in distilled water. For the treatment of burns.

### **Lotio Acidi Tannici (Mid. H.).**

Tannic acid 10 gr., resorcinol 4 gr., spirit of rosemary 1 dr., water to 1 oz. For oily seborrhœa.

**Pessus Acidi Tannici (B.P.C.)** contains 10 gr. (0.6 g.).

### **Pulvis Acidi Tannici et Acriflavinae (C.X.H.).**

Tannic acid 30 gr., acriflavine 1½ gr., warm sterile water to 3½ fl. oz. To be dissolved immediately before use and applied with a sterile brush, or on gauze, or as a spray.

### [P2-S1] **Solvellæ Acidi Tannici Compositæ (B.P.C.).**

One solution-tablet dissolved in 1 fl. oz. of water gives a solution of about the same strength as the B.P.C. lotion.

**Suppositorium Acidi Tannici (B.P.).**

3 grains (unless otherwise stated), with theobroma oil *q.s.* to 15 grains.

[D-P1-81] **Suppositories of Tannic Acid with Opium**, 1 grain in addition, or [D-P1-81] morphine  $\frac{1}{2}$  gr.

**Trochiscus Acidi Tannici (B.P.).** Each contains  $\frac{1}{2}$  grain (0.03 g.).

**Unguentum Acidi Tannici (B.P.).**

Tannic acid 20, in glycerin, yellow beeswax and benzoinated lard to 100.

*B.P. Add. II* allows the following alternative formula:—tannic acid 20 g., glycerin 20 g., simple ointment, prepared with yellow soft paraffin, 60 g.

**Unguentum Acidi Tannici (U.S.P. XI).**

Tannic acid 20, glycerin 20, wool fat 3, yellow wax 3, petrolatum 54.

**Eldoform (Bayer Products, London).** A yeast compound of tannic acid in  $7\frac{1}{2}$  gr. tablets. *Dose.*—1 or 2 tablets 3 to 4 times daily; children,  $\frac{1}{2}$  tablet 3 or 4 times daily. Anti-diarrhoeic in diarrhoea and dysentery.

[P1] **Tanichthol Suppositories (Sharp & Dohme, London).** Contain tannic acid  $2\frac{1}{2}$  gr., phenol  $\frac{1}{2}$  gr., ichthyol 1 gr., extracts of stramonium, belladonna and witch hazel of each  $\frac{1}{2}$  gr. in a glycerin base. Haemorrhoids, anal fissure and fistula, and chronic inflammatory conditions of the rectum, anus and vagina.

**Aluminii Tannas. Syn. TANNAL INSOLUBILE.**

$\text{Al}_2(\text{OH})_3(\text{C}_{12}\text{H}_9\text{O}_6)_2 \cdot 10\text{H}_2\text{O}$ . Is made by precipitating a solution of aluminium trisulphate with sodium tannate, or better by treating freshly made aluminium hydroxide with tannin solution. As astringent for chronic catarrh of the respiratory organs.

**Albuminum Tannicum (U.S.P. XI, P. Belg. IV, P. Jap., F.E. VIII, P. Austr., P. Ned. V with method of making). Prop. Name.** TANNALBIN (Knoll, London; Savory & Moore, London).

*Dose.*—8 to 15 grains (0.5 to 1 g.). *U.S.P. XI* average dose 30 grains.

A compound of tannin with albumen. A pale brown, insoluble, tasteless powder.

**Uses.** A disinfectant soluble in the intestines but unaffected by the stomach, given for diarrhoea.

**Tannocarbon (Richter, London).** Tablets containing tannin albuminate 2 gr., charcoal 2 gr. *Dose.*—1 or 2 tablets thrice daily. Flatulence, dysentery, mucous colitis.

**Zinci Tannas. Syn. "SEL DE BARNIT."**

Is obtained by treating zinc oxide 10 in water 15 with tannin 50 in alcohol (45%) 100. Dry at gentle heat. Used as ophthalmic application and for bed sores and other skin lesions.

**Acetannin (B.P.C., Fr. Cx., P.G. VI, etc.). Syn. and Prop. Name.** DIACETYL-TANNIN, ACIDUM ACETYLTANNICUM, TANNYL ACETATE, TANNIGEN (Bayer Products, London), TANNINUM ACETYLICUM (P. Jap. V).

$\text{C}_{14}\text{H}_8(\text{COCH}_3)_2\text{O}_6 = 406.1$ .

*Dose.*—5 to 10 grains (0.3 to 0.6 g.) in cachet.

A yellowish or greyish white tasteless powder. Almost *insoluble* in water, alcohol or ether; soluble in ethyl acetate, and in alkalis

with decomposition. *P.G. VI* defines it as mainly a mixture of diacetyl and triacetyltannin.

In diarrhœa. Dissolves in the intestine, appearing in the urine as gallic acid. Should not be prescribed with alkali, or combined with hot fluids.

**Methyleneditannin** (*P.G. VI*). *Syn. and Prop. Name.* METHYLDITANNIN, TANNIFORM (*Merck, Darmstadt; Savory & Moore, London*).

A compound of tannin with formaldehyde in reddish-white powder, insoluble in water, soluble in alcohol and alkalis. Used as an antiseptic in ointment (1 in 10) or dusting powder, alone or with 1 to 4 parts of starch, for bedsores, hyperhidrosis, pruritus, eczema (particularly in interdigital eczema), piles and tender feet. Internally in diarrhœa and enteritis, in doses of 8 to 15 gr.

**Acidum Gallicum** (*B.P.C., P. Helv. V, P. Jap. V*). *Syn.* ACIDO AGALICO (*F.E. VIII*).  $C_6H_2(OH)_3 \cdot COOH, H_2O = 188.1$ .

*Dose.*—5 to 15 grains (0.3 to 1 g.).

Crystals or crystalline powder of brownish colour.

**Soluble** about 1 in 100 of water, 1 in 3 of boiling water, 1 in 40 of ether, 1 in 6 of warm glycerin, 1 in 3 of alcohol 90%; insoluble in benzene and chloroform. Properties and uses similar to those of tannic acid, *q.v.*

**Glycerinum Acidi Gallici** (*B.P.C.*).

*Dose.*—10 to 60 minims (0.6 to 4 ml.).

About 1 in  $6\frac{1}{2}$  w/w. Used in the same way as Glycerinum Acidi Tannici.

**Galla** (*B.P.C., U.S.P. XI, Fr. Cx., P. Helv. V, P. Dan.*).

*Dose.*—10 to 20 grains (0.6 to 1.2 g.). *U.S.P. XI* average dose 8 grains.

Excrescences on *Quercus infectoria* (Fagaceæ) caused by deposition of eggs of *Cynips gallæ tinctoriæ* (Cynipidæ). Astringent. Contains 50 to 70% of gallotannic acid.

**Tinctura Gallæ** (*B.P.C.*). *Dose.*— $\frac{1}{2}$  to 2 drachms (2 to 8 ml.). 1 in 8 of alcohol 60%.

**Unguentum Gallæ** (*B.P.C.*). 20%.

**Unguentum Gallæ** (*U.S.P. XI*).

Nutgall 20, wool fat 5, yellow wax 5, petrolatum 70.

[P1-81] **Unguentum Gallæ cum Opio** (*B.P.C.*). Unguentum Gallæ (*B.P.C.*) with addition of  $7\frac{1}{2}$ % of powdered opium. (*Exempt [D]*).

**Skol** (*Skol Products, London*). Extract of galls 5, menthol 0.25, phenol 0.5, glycerin 3, salicylic acid 1, alcohol and water to 100. A healing antiseptic for use in burns, bed-sores, cuts, stings, etc.

**Æsculus Hippocastanum**. *Syn.* HORSE CHESTNUT, MARRON D'INDE (*Fr. Cx.*). Tincture of seeds 1 in 10 of proof spirit has been given for painful hæmorrhoids. *Dose.*—10 minims night and morning. A liquid extract has been used, painted on or rubbed in, in rheumatism and neuralgia.

**Alcoolature de Marron d'Inde Stabilisé** (*Fr. Cx.*). Horse chestnuts (1-1) and alcohol 75% are refluxed for two periods of 20 minutes, filtered, and any lost weight adjusted.

**Æsculin**,  $C_{21}H_{32}O_{11} \cdot \frac{1}{2}H_2O = 367.1$ , a glycoside, soluble in water to which 2 to 3% sodium carbonate is added, also soluble in alcohol. Solutions have a blue fluorescence, and have been used similarly to quinine in X-ray and Finsen light treatment (*q.v.*).

An ointment containing æsculin 2% in soft paraffin or other base may be used for prevention of sunburn.

**Hæmatoxylin** (B.P.C.). *Syn.* LOGWOOD. The unfermented heart-wood of *Hæmatoxylon campechianum* (Leguminosæ). Contains 10% of hæmatoxylin, and tannin. Is used as an astringent, and the decoction is also used for some forms of urinary hæmorrhage.

Preparations of logwood colour the fæces and urine red, and stain linen. The fermented chips used by dyers are deep red in colour, have lost the sweet taste and the hæmatoxylin is oxidised to hæmatein,  $C_{14}H_{12}O_4$ .

**Decoctum Hæmatoxyli** (B.P.C.). *Dose.*— $\frac{1}{2}$  to 2 ounces (15 to 60 ml.). 1 in 20 with 1% of cinnamon.

**Extractum Hæmatoxyli Liquidum** (B.P.C.). *Dose.*— $\frac{1}{2}$  to 2 drachms (2 to 8 ml.). 1 in 1.

**Hæmatoxylin.**  $C_{16}H_{14}O_4 \cdot 3H_2O = 356.2$ . Usually in yellowish granular crystals, slowly soluble in water, easily in alcohol. Alcoholic solution 0.2% is used as indicator—yellow in acid and purple in alkaline solution.

**Decoctum Sappan.** 1 in 20 of sappan wood, *Cesalpinia Sappan* (Leguminosæ), is similar to decoction of logwood.

**Myrobalanum** (B.P.C.). *Syn.* BLACK OR CHEBULIC MYROBALANS. The dried immature fruits of *Terminalia Chebula* (Combretacæ). Contain 20 to 40% of tannin. Used as an equivalent of gall in India and the East.

It is a valuable styptic. Is purgative in large doses ( $\frac{1}{2}$  to 2 dr.), but may constipate after purging. The natives employ it in perineal injuries caused during childbirth, also in eczematous sores and prolapsus ani.

Unguentum Myrobalani and Unguentum Myrobalani cum Opio are similar to the corresponding preparations of gall.

**Quercus** (B.P.C.). *Syn.* OAK BARK. The dried bark of the British oak, *Quercus Robur* and *Q. sessiliflora* (*Q. sessiliflora* and *Q. pedunculata*, *P. Helv. V*) (Fagacæ). Contains 15 to 20% of quercitannic acid.

**Decoctum Quercus** (B.P.C.). About 1 in 15. Has been used as a rectal injection for hæmorrhoids and as an astringent gargle.

## ACIDUM TARTARICUM

B.P., U.S.P. XI, *Fr. Cx.*, *P. Jap. V*, *P. Helv. V*, *P. Dan.*

$(CHOH \cdot COOH)_2 = 150.05$ .

*Dose.*—5 to 30 grains (0.3 to 2 g.).

Colourless crystals or a white powder obtained from potassium acid tartrate. It is odourless and has a strongly acid taste.

**Soluble** 10 in 8 of water, 1 in  $2\frac{1}{2}$  of alcohol 90%, 1 in  $4\frac{1}{2}$  of glycerin, 1 in 120 of ether 0.720, 1 in 5 of dehydrated alcohol. Nearly insoluble in benzene and chloroform.

**Incompatible** with carbonates, and with potassium, calcium and mercury salts.

**Antidotes.** Give calcium hydroxide or magnesium hydroxide, stirred up in water, freely. Empty stomach by stomach tube, using lime water. Purgative dose of castor oil.

**Uses.** For making effervescent preparations, effervescent tablets, and cooling drinks. If not neutralised, it must be taken well diluted.

**Ammonii Tartras.**  $(CHOH \cdot COONH_4)_2 = 184.1$ .

White efflorescent crystals soluble in water.

**Liquor Ammonii Tartratis** (R.L.O.H.).

Contains 20 or 40 gr. of neutral ammonium tartrate per oz. of sterilised water. For treatment of lime burns of the eye by irrigation.

**LIME BURNS OF THE EYE.** Daily irrigation for a period of 15 minutes with a 10% solution of neutral ammonium tartrate recommended. Stated to dissolve the calcium carbonate formed in the tissue.

**Potassii Tartras** (*B.P.C.*, *P.G. VI*, *P. Jap. V*). *Syn.* NORMAL OR NEUTRAL POTASSIUM TARTRATE.

$(\text{CHOH} \cdot \text{COOK})_2 \cdot \frac{1}{2} \text{H}_2\text{O} = 235.3$ .

*Dose.*— $\frac{1}{2}$  to 4 drachms (2 to 16 g.).

Crystalline powder with bitter taste made by neutralising acid potassium tartrate with potassium carbonate. Has purgative and diuretic properties.

*Soluble* about 5 in 3 of water.

**Potassii Tartras Acidus** (*B.P.*, *Fr. Cx.*, *P. Helv. V*). *Syn.* POTASSII BITARTRAS (*U.S.P. XI*), PURIFIED CREAM OF TARTAR.  $\text{COOH} \cdot (\text{CHOH})_2 \cdot \text{COOK} = 188.1$ .

*Dose.*—15 to 60 grains (1 to 4 g.). *U.S.P. XI* average dose 30 grains.

Obtained by recrystallising the crude tartar (argol) deposited during the fermentation of grape-juice. A white powder with acid taste *soluble* 1 in 220 of water, 1 in 16 of boiling water, insoluble in alcohol 90%.

*Uses.* A saline purgative producing a watery motion in  $\frac{1}{2}$  to 2 hours. It is also a diuretic and is especially useful in renal dropsy and in ascites from hepatic disease; for this purpose it is usually employed in the form of Imperial Drink (*vide infra*). In large and repeated doses it renders the urine alkaline and is of value in *B. coli* infections of the urinary tract.

**Collutorium Acidi Tartarati** (*R.D.H.*).

Potassium acid tartrate 2 gr., tartaric acid 1 gr., syrup of lemon 3 m., saccharin  $\frac{1}{2}$  gr., water to 1 oz. Use 1 tablespoonful in half a tumblerful of water.

**Potus Imperialis** (*B.P.C.*). *Syn.* HAUSTUS IMPERIALIS.

Contains 2 grains of potassium acid tartrate per fl. ounce, with citric acid, oil of lemon, tincture of lemon and water.

*U.C.H.* has potassium acid tartrate 1 dr., sugar 4 dr., boiling water 1 pint. *Mid. H.*—Potassium acid tartrate 1 dr., tartaric acid 10 gr., soluble saccharin 1 gr., oil of lemon 3 m., water to 20 oz. *L.H.*—Potassium acid tartrate 40 gr., lemon juice  $\frac{1}{2}$  oz., syrup  $\frac{1}{2}$  oz. (omit for diabetic patients), water to 20 oz. *K.C.H.*—Potassium acid tartrate 1 dr., tartaric acid 1 dr., oil of lemon 1  $\frac{1}{2}$  m., sugar 2 oz., boiling water 20 oz.

**Potassii Borotartras** (*Fr. Cx.*). *Syn.* SOLUBLE CREAM OF TARTAR.

*Dose.*—20 to 40 grains (1.2 to 2.5 g.).

An amorphous white powder prepared by dissolving potassium bicarbonate in boiling water, adding tartaric acid and boric acid, filtering, evaporating and drying off at 40°.

*Soluble* 1 in 1 of water.

Epilepsy has been treated with it—as much as 3 g. daily, sometimes combined with bromide. It is said to give better results when combined with phenobarbitone than either separately, commencing with 1.5 g. borotartrate and 0.15 g. phenobarbitone daily in 3 doses, continued for 3 years.



**Sodii et Potassii Tartras** (B.P., U.S.P. XI, P. *Helv. V*, P. *Dan.*). *Syn.* ROCHELLE SALT, SEIGNETTE SALT, SODA TARTARATA.  $\text{COONa} \cdot (\text{CHOH})_2 \cdot \text{COOK} \cdot 4\text{H}_2\text{O} = 282.2$ .

*Dose.*—2 to 4 drachms (8 to 16 g.).

Colourless crystals. *Soluble* 1 in  $1\frac{1}{2}$  of water; almost insoluble in alcohol 90%.

*Uses.* A saline cathartic and diuretic with an alkalinising action on the urine. It is employed in dropsy and rheumatism, and as a mild purgative, and is the chief constituent of Seidlitz Powder.

**Pulvis Effervescens Compositus** (B.P.). *Syn.* SEIDLITZ POWDER, PULVIS SODÆ TARTARATÆ EFFERVESCENS.

Sodium potassium tartrate, in dry powder, 7.5 g., sodium bicarbonate, in dry powder, 2.5 g., in the blue paper. Tartaric acid, in dry powder, 2.5 g., in the white paper.

**Pulvis Effervescens Compositus Duplex** (B.P.C.). *Syn.* DOUBLE-STRENGTH SEIDLITZ POWDER.

Contains  $231\frac{1}{2}$  grains (15 g.) of sodium potassium tartrate, double the amount in the B.P. Seidlitz Powder.

**Pulvis Effervescens Compositus Fortis** (B.P.C.). *Syn.* EXTRA-STRONG SEIDLITZ POWDER.

Contains 173½ grains (11.25 g.) of sodium potassium tartrate, 50% more than the amount in the B.P. Seidlitz Powder.

**Pulveres Effervescentes Compositi** (U.S.P. XI).

Each blue paper contains 150 gr. of a mixture of 1 part of sodium bicarbonate and 4 parts of Rochelle salt, and each white paper contains 32½ gr. of tartaric acid.

**Citralka** (*Parke, Davis, London*). Combination of the citrates and tartrates of sodium and potassium together with salts of magnesium, calcium and lithium. *Dose.*—1 or 2 discs dissolved in a glassful of cold water, every 3 hours.

**Salvitæ** (*American Apothecaries Co., New York; Coates & Cooper, London*). Strontium lactate 0.3, lithium carbonate 0.15, caffeine and quinine citrate 0.8, "sodii-forma-benzoas" 1.6, calcium lactophosphate 0.15, sodium and potassium citrotartrate 59.0, magnesium sulphate 8.0, sodium sulphate 30.0. *Dose.*—A teaspoonful in a glass of water every 4 hours. Colds and influenza.

**Sodii Tartras (Neutrale)**.  $(\text{CHOH} \cdot \text{COONa})_2 \cdot 2\text{H}_2\text{O} = 230.06$ .

*Dose.*—As aperient  $\frac{1}{2}$  to 1 ounce. Diuretic, 15 to 60 grains repeated. White crystalline powder comparatively tasteless. Soluble in water 1 in 2. Relaxes the bowels and increases the flow of urine.

**Limonade Tartro-sodique** (*Fr. Cx.*). A solution of sodium tartrate, saturated with carbon dioxide and sweetened.

**Acidum Malicum**. *Syn.* HYDROXYSUCCINIC ACID.

$\text{C}_3\text{H}_3(\text{OH})(\text{COOH})_2 = 134.0$ .

*Dose.*—1 to 5 grains (0.06 to 0.3 g.).

White deliquescent crystals *soluble* in water 1 in 1, and in alcohol 1 in  $1\frac{1}{2}$ . Has been used as throat spray in diphtheria and other throat affections. Possesses properties similar to those of tartaric acid. In phthisis much larger doses—up to 2 drachms—have been given.

**Extractum Ferri Pomati** (*P. Jap. V*) is made from sour ripe apples and iron powder, and contains 5% of Fe.

## ACONITUM

*B.P., Fr. Cx., U.S.P. XI, P. Helv. V, F.E. VIII, etc.*

[P1] "*Alkaloids, the following; their salts, simple or complex:—Aconite, alkaloids of.*"

[81] "*Alkaloids, the following; their salts, simple or complex:—Aconite, alkaloids of, except substances containing less than 0.02 per cent. of the alkaloids of aconite.*"

[86] "*Alkaloids—Aconite, alkaloids of—specify proportion in a preparation as the proportion of any one alkaloid of aconite that the preparation would be calculated to contain on the assumption that all the alkaloids of aconite in the preparation were that alkaloid.*"

*Dose.*—No dose is given in *B.P.* *Fr. Cx.* has max. single dose 0.1 g., max. in 24 hours 0.3 g.; *F.E. VIII* has 0.01 g. and 0.05 g. respectively. *U.S.P. XI* average dose 1 grain.

The dried root of *Aconitum Napellus* (Ranunculaceæ). *B.P.* '32 gives no standard for alkaloidal content. *B.P.* '14 required not less than 0.4% of ether-soluble alkaloids.

**Antidotes.** Empty stomach by emetic, or by using stomach tube with 180 gr. of tannic acid in 2 gallons of water. Give 20 gr. tannic acid in 6 oz. of lukewarm water, followed by medicinal charcoal, stirred up in water. Keep patient warm, and lying down with the head rather low. Give 1 dr. of aromatic spirit of ammonia, well diluted, every 15 minutes. Strychnine,  $\frac{1}{2}$  gr., hypodermically. Atropine sulphate,  $\frac{1}{100}$  gr., and digitalin,  $\frac{1}{100}$  gr., hypodermically, have been recommended. Artificial respiration may be necessary over a long period. Oxygen inhalations.

**Uses.** Anodyne, diaphoretic, diuretic.

*Externally* the liniment, as such, or mixed with chloroform or belladonna liniment in neuralgia and rheumatism (causes tingling and numbness). Equal parts of strong tincture of aconite and of weak solution of iodine make a useful application in dental periostitis.

*Internally* the tincture diminishes the force and rate of the pulse, especially in the early stages of fevers and mild local inflammations, such as feverish cold, laryngitis, and first stages of pneumonia and erysipelas. It also relieves the pain of neuralgia, pleurisy and aneurism. Acute tonsillitis in children is well treated by aconite; for a child 5 to 10 years old, 1 to 2 minims of tincture.

Aconite in small but frequent doses will often abort a quinsy. A useful prescription is:—Tincture of aconite 1 m., phenazone 1 gr., caffeine citrate 5 gr., water to 1 oz. To be taken every hour for eight hours.—D. McKenzie, *Practitioner*, 1935, 656.

[P1-S1] **Aconitum Folium** (*B.P.C.*), *syn.* MONKSHOOD OR WOLFSBANE, consists of the dried leaves and flowering tops. It contains 0.1 to 1% of alkaloids.

*Fr. Cx.* employs fresh leaves for making Alcoolature d'Aconit, 1 = 1, using 95% alcohol for macerating 8 days. To contain 0.1% alkaloids. Max. single dose 1 g., max. daily dose 5 g.

[P1-S1] **Chloroformum Aconiti** (*B.P.C.*). 1 = 1, prepared by percolating aconite moistened with ammonia with chloroform and alcohol.

**[P1-S1] Collodium Anodynum (B.P.C.).**

Aconite about 0.1% *w/v* and veratrine about 0.7% *w/v* in acetone and acetone collodion.

**[P1-S1] Extractum Aconiti Siccum (P. Belg. IV).**

Prepared from the root with 70% alcohol and standardised to 1% of alkaloids. *Max. single dose.*— $\frac{1}{4}$  grain. *Max. during 24 hours* 1  $\frac{1}{2}$  grains approx. *F.E. VIII* is assayed biologically. *P. Ital. V* contains 0.5% of alkaloids.

**[P1-S1] Linimentum Aconiti (B.P.). 1 in 2.**

Prepared by percolating the root with alcohol 90% and dissolving 3% *w/v* of camphor in the percolate. Useful in neuralgia. *It is not suitable for painting on the gums.*

**[P1-S1] Linimentum Aconiti Oleosum (B.P.C.). Syn. A.B.C. LINIMENT.**

Liniment of aconite, liniment of belladonna, liniment of chloroform equal parts. To be well shaken before use, as the olive oil in the chloroform liniment is not soluble in the other ingredients. *See also* Pigmentum Aconiti Compositum.

The oil in the "A.B.C." formula seems to be essential—otherwise the preparation proves too irritant for sensitive skins.

**Antidotes.** Treat as for poisoning by aconite, *see* p. 120.

**POISONING.** Acute aconite poisoning due to accidental swallowing of an ounce of A.B.C. liniment successfully treated by intravenous injection of 3 pints of hypertonic saline after all the usual measures had failed. All the symptoms abated and recovery was complete in 72 hours.—M. Talukder, *Indian med. Gaz.*, 1935, 628.

**[P1] Mist. Aconiti (N.I.F.).**

Tincture of aconite 1 m., tincture of belladonna 3 m., dilute hydrochloric acid 5 m., solution of mercuric chloride 10 m., water to  $\frac{1}{2}$  oz.

**[P1-S1] Pigmentum Aconiti Compositum (B.P.C.).**

Liniment of aconite and liniment of belladonna, of each 37  $\frac{1}{2}$ % with chloroform and distilled water. A non-oily form of A.B.C. liniment. The water is necessary to produce a non-separable preparation.

**[P1-S1] Pigmentum Iodi et Aconiti (B.P.C.). Syn. TINCTURA IODI ET ACONITI.**

Equal parts of weak solution of iodine and strong tincture of aconite. Used in dental periostitis. Strong solution of iodine is sometimes used instead of the weak.

**[P1-S1] Tinctura Aconiti (B.P.C.).**

*Dose.*—2 to 5 minims (0.12 to 0.3 ml.). As a febrifuge 2 minims every 10 minutes or quarter of an hour for an hour, then repeat dose every hour till skin acts well and temperature is reduced.

Strength about 1 in 6, by percolation with alcohol 70%. It is not standardised as to alkaloidal content. *B.P. '14* standardised to 0.04% *w/v* of ether-soluble alkaloids.

**[P1-S1] Tinctura Aconiti (U.S.P. XI).**

*Average dose.*—10 minims (0.6 ml.).

A 10% tincture is prepared, adjusted to pH 3 with hydrochloric acid, and assayed biologically, using guinea-pigs and a reference sample of aconitine. It is then diluted with the menstruum and sufficient hydrochloric acid to maintain a pH of 3, so that the finished tincture has a potency per ml. equivalent to 0.14 to 0.16 mg. of the aconitine.

[P1-81] **Tinctura Aconiti Fortis** (B.P.C.), *syn.* FLEMING'S TINCTURE OF ACONITE, is about five times the strength of the ordinary tincture. Turnbull's tincture of aconite is similar. They are not used internally.

[P1-81] **Aconitina** (B.P.C., *Fr. Cx.*). *Syn.* ACETYL BENZOYLACONINE.  $C_{34}H_{47}O_{11}N = 645.4$ .

*Dose.*— $\frac{1}{800}$  grain (0.0001 g.). Larger doses, up to  $\frac{1}{300}$  grain (0.0003 g.), are sometimes given and may be increased, if desired, with extreme caution, the maximum single dose being 0.001 g.

*Fr. Cx.* gives 0.0005 g. as maximum during 24 hours; *F.E. VIII*, 0.001 g.; *P. Helv. V*, 0.0003 g.

An alkaloid obtained from aconite—content about 0.3 to 0.6% of ether-soluble alkaloids, chiefly aconitine. In colourless crystals or crystalline powder, m.p.  $196^{\circ}$  to  $200^{\circ}$  when heated rapidly. A drop of dilute solution placed on the tongue produces a characteristic tingling sensation.

*Soluble* 1 in 30 of alcohol 90%, 1 in 65 of ether, 1 in 7 of benzene, and 1 in 1 of chloroform; sparingly soluble in water.

*Antidotes, vide Aconite.*

*Uses.* Employed externally (*vide* Unguentum Aconitinæ and Oleinatum Aconitinæ) in neuralgia, *avoiding mucous membranes and raw skin*. Internally in the form of a pill is a depressant, calmative and diaphoretic, but rarely administered owing to extremely powerful cardiac action.

[P1-81] **Unguentum Aconitinæ** (B.P.C.).

Aconitine 2% in oleic acid and lard. Best freshly prepared. A piece of the size of a bean is gently rubbed in for facial neuralgia, avoiding broken skin and mucous membranes.

[P1-81] **Aconitinæ Nitras**.  $C_{34}H_{47}O_{11}N.HNO_2 = 708.4$ . *Dose.*— $\frac{1}{10}$  grain (0.0001 g.), hypodermically. *Fr. Cx.* gives 0.0005 g. as max. in 24 hours. A crystalline stable salt, soluble 1 in 10 of water and in alcohol. M.p.  $200^{\circ}$ .

[P1-81] **Granules of Aconitine** *Fr. Cx.* and of **Aconitine Nitrate** *Fr. Cx.* contain  $\frac{1}{10}$  mgr. in each, and are coloured pink.

[P1-81] **Aconitinæ Hydrobromidum**,  $C_{34}H_{47}O_{11}N.HBr.2\frac{1}{2}H_2O = 771.3$ , and [P1-81] **Aconitinæ Hydrochloridum**,  $C_{34}H_{47}O_{11}N.HCl.3H_2O = 735.9$ , are crystalline salts with dose as for the nitrate.

[P1-81] **Oleinatum Aconitinæ**.

Aconitine 2, oleic acid by weight 98. Dissolve; may be perfumed. Is painted on the skin (not when broken) for neuralgia.

[P1-81] **Poudre d'Aconitine au Centième** (*Fr. Cx.*). Aconitine 1%, carmine 2.5%, in lactose.

[P1-81] **Poudre d'Azotate d'Aconitine au Centième** (*Fr. Cx.*). Aconitine nitrate 1%, carmine 2.5%, in lactose.

**Bryonia** (B.P.C.). *Syn.* VITIS ALBA, WHITE BRYONY, ENGLISH MANDRAKE.

The dried root of *B. dioica* (Cucurbitaceæ), the only species commonly found in this country—hence called English Bryony. Contains an amorphous glucosidic bitter substance and an amorphous alkaloidal principle.

**Tinctura Bryoniæ** (B.P.C.).

*Dose.*—1 to 10 minims (0.06 to 0.6 ml.), or more. 1 in 10. Useful in pleurisy. Relieves the pain and allays the cough. In large doses it is an active cathartic, used for dropsy. The fresh plant applied to the skin will cause vesication.

**Mandragora.** Syn. MANDRAKE. *M. Autumnalis* (Solanaceæ).

The root is often forked and is sometimes similar to the human body in shape. It is poisonous, with effects allied to those of belladonna. Contains an alkaloid. Much confusion exists over the name mandrake. The Mandrake, as pharmacists understand the Museum specimens, is to be associated with *M. officinarum* L. (this includes two varieties,  $\alpha$  *vernalis*,  $\beta$  *autumnalis* = "European" Mandrake). English, or false, "Mandrake" is *Bryonia dioica*. American Mandrake is *Podophyllum peltatum*.

**Corydalis** (B.P.C.).

Dose.—5 to 15 grains (0.3 to 1 g.).

The dried tubers of *Dicentra canadensis* (Squirrel Corn, Turkey Corn) and of *D. Cucullaria* (Dutchman's Breeches) (Papaveraceæ). Reputed to have tonic and diuretic properties. Administered as a decoction.

**Bulbocapnine.**  $C_{19}H_{19}O_4N$ .

Dose.— $1\frac{1}{2}$  grains (0.1 g.) either *per os* or subcutaneously once or twice daily.

An alkaloid from *Corydalis tuberosa* and from *Dicentra canadensis*. Insoluble in water but soluble in alkalis, and precipitated from them by  $CO_2$  or ammonium chloride. Solutions oxidise slowly to a green colour.

Of value as a sedative in post-encephalitic conditions and in tremor of various origins—paralysis agitans, choreic disorders, multiple sclerosis, and hemiplegia.

Ménière's disease well treated. One tablet of 0.1 g. *per os* daily is sufficient to prevent vertigo, while the acute attack is treated by 0.1 g. hypodermically, which at once relieves.—W. S. Thacker Neville, *Brit. med. J.*, ii/1931, 54.

## ACRIFLAVINA

B.P. Add. I.

Syn. FLAVINE, ACRIFLAVINÆ HYDROCHLORIDUM (U.S.P. XI).

Acriflavina (U.S.P. XI) is identical with euflavine.

Dose.—5 grains have been given, but euflavine is more used *per os*.

Acriflavine is an orange-red to red, crystalline, odourless powder. It consists of a mixture of the hydrochloride of 2:8-diamino-10-methylacridinium chloride and diaminoacridine dihydrochloride, the latter being present to the extent of approximately one-third.

**Solubility.** 1 in about 3 of water (commercial samples vary considerably owing to variations in the proportions of the two constituents present), 1 in 40 of alcohol, 1 in 4 or less of glycerin. Insoluble in liquid or soft paraffin, oleic acid, and eucalyptol. The solubility of 2:8-diamino-10-methylacridinium chloride hydrochloride is 0.4% and of diaminoacridine dihydrochloride 0.6%. Mixtures of the two are more soluble. Concentrated aqueous solutions are brown, dilute ones lemon-yellow with green fluorescence.

For details of the solubility in water of acriflavine and its constituents, see M. Gailliot, *Quart. J. Pharm.*, 1934, 63; also G. F. Hall and A. D. Powell, *Quart. J. Pharm.*, 1936, 510.

**Compatible** with normal saline if required for immediate use, but deposits after about 24 hours. Concentrations of saline higher

than 5% give a precipitate almost at once. Compatible with 0.5% sodium citrate.

**Incompatible** with Dakin's solution, eusol and other chlorine antiseptics. Also with mercuric chloride solution (e.g., 1 in 1000 as used), also with phenol (e.g., 1 in 20 solution).

Solutions may be boiled or heated in an autoclave to 130°.

*To remove acriflavine stains from the hands, etc.*—Rub with a little dilute hydrochloric acid or with a little dilute sulphurous acid, or with sulphurous acid followed by hydrochloric acid, and then wash with water.

**Antiseptic Powers.** It is markedly antiseptic. It does not affect phagocytosis, is non-irritant, and its activity is not altered by the presence of serum or urine, though it is diminished in the presence of whole blood. Acriflavine is 20 times more powerful against *S. aureus* than mercuric chloride, and 800 times more so than phenol or chloramine.

**Uses.** The dye is advised for prompt application to wounds soon after infliction, to prevent sepsis by destruction of virulent organisms before they have time to multiply, and thus to facilitate healing by first intention. Liquor Acriflavinæ (equal in bactericidal effect on staphylococci to an 80% phenol solution) is a non-irritant and painless application to the surface of wounds.

A contaminated wound, within the first few hours of infliction, if thoroughly cleaned with 1 in 1000 solution—as much as possible being left in the cavity—may be sewn up and will heal by first intention. The same result may be expected in war wounds if similar facilities are permitted, but on the whole this is not favoured. It is better to pack the wound with the soaked gauze for 3 or 4 days after requisite surgical procedure. Suppuration may thus be aborted in many cases. Inject the solution into the surrounding tissues and muscle planes with a syringe and fine needle if there is extensive damage to the tissues.

Acriflavine is also advocated at the time of secondary operations to prevent the recrudescence of sepsis when operating in an area already affected.

**For suppurating wounds** the solution is used to swab out the open wound once or twice a day *after free drainage has been secured*. All the crevices of the wound are to be reached and sloughs, etc., removed. Then lightly pack with gauze steeped in the solution and cover with a "protective." Several ounces of the solution may be safely left in the tissues or peritoneal cavity. In cases showing spreading inflammatory conditions, it is well to inject the antiseptic into the part, and especially around the edges, with a hypodermic serum syringe.

When the infection has been practically overcome, weaker solutions, e.g., 1 : 5000, may be used, or the treatment may be intermitted for a day every few days, dry dressing being substituted in the intervals, or "stimulating" applications, e.g., brilliant green solution 1 in 1000, may be employed.

Inlet tubes may be used, but frequent periodic flushing, e.g., every 2 hours, with an aqueous solution (Carrel's method) is to be *avoided*. Gauze steeped in the solution is specially favoured, as the dressing need only be changed once or twice in 24 hours.

The emulsion is extensively used as an antiseptic dressing for plugging suppurating wounds.

The muscles round the site of an infected wound may be injected with several ounces of 1 : 1000 solution without ill effect.

**General Local Use.** Strengths ranging from 0.1 to 1% are used for treatment of local conditions of the ear, such as otorrhœa, and of the mouth and throat (sycosis, folliculitis, etc.). 1 in 4000 may be used in conjunctivitis and gonorrhœal ophthalmia, and in ophthalmic surgery to prevent septic sutures, and 1 in 1000 is used as a urethral injection in gonorrhœa, injections being made twice daily, but for this purpose euflavine, being neutral, is preferred. A 0.5 to 1% solution in alcohol is of value in various skin diseases such as crusty eczema, pyoderma and impetigo. Four-hourly compresses of 1 in 1000 solution may be applied in pemphigus neonatorum and impetigo contagiosa. It is also used alone or in conjunction with tannic acid in the treatment of burns.

**Intravenous Injection.** The preparation has been tried even to the amount of 300 ml. of 1 in 1000 solution. The injection is given slowly—at the rate of 50 ml. per minute. The method has not been largely practised. *Euflavine is preferable.*

Owing to the frequent occurrence of jaundice following intravenous acriflavine therapy, Imperial Chemical Industries Ltd., Dyestuffs Group, were asked to investigate the matter, and they have now succeeded in supplying an acriflavine (Acriflavine Intravenous) which is apparently non-toxic. Patients receiving acriflavine should always be tested for the presence of urobilinogen in the urine and the use of the drug discontinued if it is found.—E. W. Assinder, *Lancet*, i/1936, 305.

For references in the literature to toxic effects see 20th Edn., Vol. I.

**Subcutaneous and Intramuscular injections** of 5 to 10 ml. of 1 in 1000 solution have been given. It has been used hypodermically in lymphangitis.

#### References to Clinical Use of Acriflavine.

**BURNS.** A 1 in 1000 emulsion in pure sterile medicinal paraffin, applied as a dressing, preferable to tannic acid. Painless and quite harmless to the conjunctiva or any mucous surface. Burns remain clean, free of septic infection and with no tendency to scarring and contraction, and no hard scab is formed as with tannic acid.—N. H. Mummery, *Lancet*, i/1933, 662.

Daily anointing with the solution produces a film, which increases in thickness and falls off in about 10 days, leaving a marvel of healing.—W. Robertson, *ibid.*, 830.

**GANGRENE, MOIST, of arm and leg, and hernia of spleen, well treated with flavine.**—W. J. Sheehan, *Brit. Med. J.*, i/1930, 822.

**GONORRHOEA.** From the treatment of over 100 patients with acute gonorrhœa it was concluded that acriflavine given by deep subcutaneous injection will cause urethral discharge to disappear quickly, but relapses are common and local pain at site of injection makes it unsuitable for use in an out-patient clinic. Its use is not without danger. Jaundice is apt to appear after a long latent period, and deep subcutaneous injection may lead to local pain and abscess formation. It appears to lessen the incidence of complications, but has no beneficial effect when these are established.—E. Hughes and C. A. Birch, *Lancet*, ii/1933, 634.

In 4985 cases of acute gonorrhœa treated by intravenous injections of 2% acriflavine, the most noticeable feature has been the short duration of the urethral discharge, which ceases as a rule in 7 to 10 days; the duration of the actual infection is also much shortened.—E. W. Assinder, *Lancet*, i/1936, 304.

**PERINEAL DRESSINGS.** Emulsion in liquid paraffin 1 in 1000 used as a routine dressing in perineorrhaphies. The dressing renewed after each micturition. When operating for the cure of prolapse, with reasonable nursing, the wound will heal by first intention.—M. A. Dobbin Crawford, *Lancet*, ii/1929, 980; *Brit. med. J.*, i/1930, 822; see also E. M. R. Fraser, *Brit. med. J.*, ii/1930, 1066.

**RHEUMATISM.** 23 out of 33 cases cured by intravenous injection of 1 ml. of 2% solution of acriflavine hydrochloride. Two injections usually gave relief from pain. Phagocytic action. No untoward effects.—Norioka, *J. Amer. med. Ass.*, i/1929, 1022.

### **Emulsio Acriflavinae (B.P.C.).**

Acriflavine, 1 in 1000, with liquid paraffin, white beeswax and distilled water. The value of this water-in-oil emulsion has been questioned, and claims have been made for an oil-in-water preparation. In practice it has proved the best of its type, but the directions for making could be improved by substituting the following:—Melt the wax in 9 fluid ounces of the liquid paraffin and cool; add, very gradually with constant trituration, the solution of acriflavine, and finally the remainder of the liquid paraffin.

U.C.H. has acriflavine 0·1, thymol 0·005, Japan wax 3·25, liquid paraffin 76·65, water 20.

The following has also been suggested: Dissolve acriflavine 0·5 g. in warm boiled distilled water 25 ml.; sterilise wool fat 30 g., put in a sterile mortar, add the solution in small portions with stirring, and finally add liquid paraffin to 500 ml.—W. J. Clarke, *Pharm. J.*, ii/1932, 435.

The emulsion in use at the City of London Hospital is prepared as follows: Acriflavine 1 g. is dissolved in distilled water 100 ml., to this is added olive oil 100 ml., oleic acid a few drops, and saccharated solution of lime about 10 ml.; triturate to form a cream and add olive oil or liquid paraffin to produce 1000 ml. This emulsion with the addition of aromatics is being used with success in the after-care of surgical cases, such as chronic empyema and lung abscesses where there is offensive discharge and where an antiseptic deodorant dressing is indicated for plugging. 3 ml. of the following aromatic essence is added to 100 ml. of the acriflavine emulsion: guaiacol 12·5 ml., oil of eucalyptus 25 ml., thymol 6·25 g., methyl salicylate 25 ml., oil of lemon to 100 ml.—W. Trillwood, *Prescriber*, 1935, 293.

Acriflavine emulsions of both oil-in-water and water-in-oil types were tested for their germicidal activity by the wet filter paper methods. The results showed the B.P.C. preparation to have little antiseptic power, and generally oil-in-water emulsions to have greater bacteriostatic and germicidal properties than water-in-oil emulsions.—W. C. Wood, *Pharm. J.*, i/1939, 327.

Suggested formula:—Acriflavine 0·1 g., hard soap 1·25 g., water 25 ml., liquid paraffin to 100 ml. Dissolve the acriflavine in 5 ml. of the water and the hard soap in the remainder of the water, previously heated. Mix the two solutions, add the liquid paraffin and shake well.—H. W. Tomski, *Pharm. J.*, ii/1939, 447.

**Flavine-starch poultices** in the treatment of eczema. 4 tablespoonfuls of rice starch and 10 gr. of acriflavine mixed with cold water; 1 pint of boiling water added, and the mixture boiled till it thickens. When nearly cold pour on to dressing cloth, to form a layer  $\frac{1}{4}$  inch thick. When cold and set, cover with a layer of gauze and apply to part. Change 3 or 4 times a day and bathe part at each change with acriflavine 1 in 1000 in 0·85% NaCl. Resistant cases of seborrhoeic eczema successfully treated by this method.

**Glycerin. Acriflavin. (N.I.F.).** Acriflavine 3½ gr., glycerin to 4 fl. oz.

The Committee on Pharmacy and Pharmacognosy of the Pharmacopœia Commission (*Report* 13) have recommended the inclusion in the B.P. of glycerin of acriflavine (1%) to be used as a stock solution for dilution with water to prepare lotion of acriflavine containing 0·1% of acriflavine.

**Guttæ Acriflavinae ex Alcohole (Mid. H.).**

Acriflavine 0·1, alcohol 90% 50, water to 100. For otorrhœa.



**Acriflavine Eye Drops.** Acriflavine 1, distilled water 200, white wax 5, castor oil to 1500. Melt the white wax in the castor oil and triturate with a warm solution of the acriflavine in the water.—P. M. Wright, *Pharm. J.*, i/1936, 248.

**Liquor Acriflavinae (B.P.C.).**

Acriflavine, 1 in 1000, in normal saline.

**Lot. Flavin. Conc. (N.I.F.).** Acriflavine 7 gr., sodium chloride 31½ gr., distilled water to 8 oz. For use dilute with an equal quantity of hot water.

**Pessus Acriflavinae (B.P.C.)** contains ½ gr. (0.008 g.).

**Tabellae Acriflavinae (B.P.C.)** contain ½ gr. (0.03 g.) in chocolate basis.

**Acriflex (Allen & Hanburys, London).** An oil-in-water emulsion containing acriflavine 0.1, glycol 3.0, perfume 0.05, stearate cream to 100.0. A non-greasy application for wounds.

**Burnol (Boots, Nottingham).** An antiseptic cream having the following formula:—Acriflavine 0.22, thymol 0.01, cera alb. 32.0, distilled water 40.0, liquid paraffin 137.25. For use in burns and scalds, ulcers and wounds, skin infections and all types of ophthalmia.

**Flavogel (Glaxo Laboratories, London).** Acriflavine 1 to 1000 in a water-soluble jelly base for use in the treatment of wounds, local septic lesions, etc., and as a catheter lubricant. Stated to be an improvement on emulsions of acriflavine, since the base is emollient and enables the antiseptic action of the dye to be more readily exerted than with the usual greasy basis.

**Euflavina (B.P.C.).** *Syn. and Prop. Name.* ACRIFLAVINA (U.S.P. XI), ACRIDINUM HYDROCHLORICUM (*Fr. Cx.*), NEUTRAL ACRIFLAVINE, NEUTROFLAVIN, TRYPAFLAVIN (*Bayer Products*), *Lond.*; not available in Gt. Britain).

**Dose.**—Internally ½ to 1 grain (0.03 g. to 0.06 g.) in tablets "enteric-coated."

An orange- or brownish-red powder prepared from acriflavine by neutralisation and precipitation with sodium chloride. Euflavine consists of a mixture of 2 : 8-diamino-10-methylacridinium chloride,  $C_{14}H_{14}N_3Cl = 259.6$ , and diaminoacridine monohydrochloride,  $C_{13}H_{12}N_3Cl = 245.6$ . The latter is usually present to the extent of between 30 and 40%.

This substance, being more basic than acriflavine, is even less irritant to mucous tissues and more suited for use *intravenously*.

**Soluble** in water, 1 in 4 of warm water, slightly soluble in alcohol 90%, almost insoluble in ether, chloroform and oils.

**Uses.** As for acriflavine. Stronger solutions can be employed. For *local use* to wounds 1 in 1000 to 1 in 500. For *bladder irrigation* and *urethral injection* 1 in 4000 to 1 in 1000. For skin infections 1% in alcohol.

*Intravenously* 1 in 1000 to 1 in 200 in lymphangitis, enlarged tuberculous glands and threatened sepsis. 50 to 100 ml. of this has been given. 50 to 100 ml. of 1 in 200 solution, in rheumatic fever, influenza, pneumonia, endocarditis, puerperal fever, septic abortion, erysipelas, etc.; 1 in 500 to 1 in 100 in gonorrhœa.

**Carbasus Euflavinae (B.P.C.).** Euflavine Gauze. 0.1%.

**Linteum Euflavinae (B.P.C. Supp.).** Euflavine lint is absorbent lint impregnated with about 0.1% of euflavine.

**Curatio Normalis X** (*B.P.C. Supp.*). *Syn.* STANDARD DRESSING No. 10, FINGER BURN DRESSING, EUFLAVINE FINGER DRESSING.

The dressing consists of an open finger-stall, made from two pieces of euflavine lint each 2 inches by  $1\frac{1}{2}$  inches, sewn to an open-wave bandage measuring 1 inch by 24 inches.

**Curatio Normalis XI** (*B.P.C. Supp.*). *Syn.* STANDARD DRESSING No. 11, MEDIUM BURN DRESSING.

The dressing consists of a pad sewn to an open-wave bandage measuring  $1\frac{1}{2}$  inches by 2 yards. The pad, which measures about 3 inches by 4 inches, is composed of a piece of euflavine lint 3 inches by 4 inches, superimposed on about 25 gr. of cotton-wool.

**Curatio Normalis XII** (*B.P.C. Supp.*). *Syn.* STANDARD DRESSING No. 12, LARGE BURN DRESSING.

This dressing is similar to Standard Dressing No. 11, but the pad measures 4 inches by 6 inches, and is composed of euflavine lint 4 inches by 6 inches, superimposed on about 50 gr. of absorbent cotton-wool. The open-wave bandage measures 3 inches by  $2\frac{1}{2}$  yards.

**Tabellæ Euflavinæ** (*B.P.C.*) contain  $\frac{1}{2}$  gr. (0.03 g.) in chocolate basis.

**Gonacrine** (*Pharmaceutical Specialities (May & Baker) Ltd., London*). Ampoules containing 5 ml. of 2% solution of euflavine for intravenous use, and  $\frac{1}{2}$  grain enteric-coated euflavine tablets for use in gonorrhœa and urinary tract infections.

**Panflavin Tablets** (*Bayer Products, London*) contain as active principle 0.003 g. of Trypaflavin. *Dose.*—1 or 2 to be sucked hourly as influenza prophylactic and in inflammatory and ulcerative conditions of the mouth and throat.

**Planacrine** (*Pharmaceutical Specialities (May & Baker) Ltd., London*). Euflavine lozenges 3 mg. flavoured with glycyrrhizin. Mouth and throat disinfection.

**Homoflavine** is the hydrochloride of 3:7-dimethyl-2:8-diamino-10-methylacridinium chloride. Closely resembles acriflavine.

**Proflavina** (*B.P.C.*). *Syn.* 2:8-DIAMINOACRIDINE SULPHATE.  $C_{13}H_{11}N_3 \cdot H_2SO_4 = 307.2$ .

An orange-red to brownish-red powder. The concentrated aqueous solution is brown. It stains the skin yellow similarly to acriflavine. Dilute solution is also light yellow with greenish fluorescence.

**Solubility.** 1 in 300 of water, 1 in 48 of alcohol 90%, 1 in 10 or less of glycerin, insoluble in liquid paraffin, oleic acid, soft paraffin and eucalyptol.

**Compatible** with normal saline solution as distinct from acriflavine (*q.v.*).

**Antiseptic Powers.**—This compound resembles acriflavine in being strongly bactericidal for all the common pathogenic bacteria. As weak a solution of proflavine as 1:200,000, it is stated, will kill *Staphylococcus aureus* in the presence of serum.

The general toxicity of proflavine for mice as tested by subcutaneous injection, and the irritating effect of concentrated

solutions on the conjunctiva, are markedly less than those of acriflavine. They may be applied to the peritoneum with safety.

**Uses.** Similar to those of acriflavine, but it is stated to differ in that it exerts a degree of hæmostatic action.

Since acriflavine, when freed from tarry matter and other impurities, becomes only sparingly soluble in water, there ceases to be any reason in preferring it, a mixture, to proflavine, a pure chemical. Their antiseptic powers are equivalent whilst proflavine has only a quarter of the mammalian toxicity of acriflavine and is less irritating to the tissues. Formulæ are put forward containing proflavine base and proflavine sulphate with a view to rendering them more readily available for therapeutic use.—A. Albert and C. Bennett, *Aust. J. Pharm.*, 1939, 175.

A 1 in 1000 solution of proflavine in isotonic saline is practically harmless to living brain tissue, whereas euflavine or acriflavine in the same concentration causes necrosis and hæmorrhage.—D. S. Russell and M. A. Falconer, *Proc. R. Soc. Med.*, 1940, 33, 394.

**Proflavine Tablets** 0·87 grain (with sodium chloride) make 2 ounces of 1 in 1000 solution; also 1·75 grains with sodium chloride to produce 4 ounces of solution.

**Proflavine Bougies.** Contain  $\frac{1}{2}$  grain (0·03 g.) in oil of theobroma; 4 inches long.

**Lotio Proflavinæ (Pro Oculis).** Proflavine 1 grain in 10 ounces. Useful in ophthalmic surgery. 1 in 1000 non-irritating, but 1 in 4000 is strong enough.

**Proflavine Oleate.** Proflavine oleate in a strength of 1% in liquid paraffin is a valuable antiseptic for the control of local sepsis in radium therapy, and is particularly useful in the radiological treatment of carcinoma of the cervix and of malignant lesions involving the skin; in the former case, it is used by means of saturating the packing by which the radium is kept in position, and in the latter by means of preliminary dressings to dry up the septic discharge and render the part clean enough for the operation.—A. A. Charteris, *Lancet*, ii/1937, 627.

**Isoflav (Boots, Nottingham).** Solution tablets of proflavine sulphate prepared so that one tablet dissolved in 4 fl. oz. of distilled water makes a 1 in 1000 isotonic buffered solution at approx. pH 6·3. An antiseptic solution for the prevention and control of wound infection in all delicate tissues, and especially for infected wounds of the brain.

**Rivanol (Bayer Products, London)** is 2-ethoxy-6 : 9-diaminoacridine lactate. A yellow dyestuff soluble about 1 in 15 of water, incompatible with acids and normal saline and unstable in solution with Novocain and Decicain.

Used in 1 in 2000 to 1 in 500 solution as an antiseptic for wounds, puerperal infection, furunculosis and for antisepsis of the abdominal cavity. For injection for deep antisepsis requires 0·25 to 0·5% of procaine hydrochloride.

## ADEPS LANÆ

*B.P., U.S.P. XI, P. Ital. V, P. Helv. V, P. Jap. V, etc.*

*Syn.* ANHYDROUS LANOLIN, LANOLÉINE (*Fr. Cx.*), WOOL FAT.

The purified yellowish cholesterin fat of sheep's wool, m.p. about 40°. Sheep's wool yields from 10 to 30%.

**Soluble** 1 in 25 of ether, 1 in 18 of oil of turpentine (both with some residual matter), almost insoluble in alcohol 90%.

Adeps Lanæ can only be saponified by alcoholic solutions of potassium hydroxide under pressure—paraffin can be easily detected by this means.

**Adeps Lanæ Hydrosus (B.P.).** *Syn.* HYDROUS WOOL FAT, LANOLIN, LANOLÉINE HYDRATÉE (*Fr. Cx.*).

Wool fat 7, distilled water 3. Melt and mix. *U.S.P. XI, Fr. Cx., P. Jap. V, P. Belg. IV and P. Ned. V* have 25% of water. *P. Ital. V* has wool fat 30, liquid paraffin 6, water 10.

Yellowish white ointment basis. More water, up to about equal weights of fat and water, may be incorporated with it without affecting its consistence. Soluble partly in alcohol, while ether and chloroform dissolve only the fats it contains.

Unmixed wool fat is not readily absorbed by the skin, but when mixed with olive oil or soft paraffin absorption is much more rapid and the stickiness greatly reduced. These mixtures may be mixed with considerable proportions of aqueous liquids forming water-in-oil emulsions, the wool fat serving as the emulsifying agent. It helps absorption of narcotic extracts, quinine, iodine, potassium iodide and chaulmoogra oil.

When an ointment containing mercuric chloride or phenol is ordered, it is usually intended for antiseptic purposes, therefore the *anhydrous* should be used, otherwise caustic action may result.

**Unguentum Adipis Lanæ (B.P.C.).** *Syn.* UNGUENTUM LANOLINI ANHYDROSI. Equal parts of wool fat and yellow soft paraffin.

**Unguentum Adipis Lanæ Compositum (B.P.C.).**

*Syn.* UNGUENTUM LANÆ COMPOSITUM, EMOLLIENT OINTMENT. Lard and wool fat, 40% of each, and yellow paraffin ointment 20%.

Simple ointment is a suitable substitute for lard in this ointment.

**Unguentum Adipis Lanæ Hydrosi (B.P.C.).** *Syn.* UNGUENTUM LANOLINI. Equal parts of hydrous wool fat and yellow soft paraffin.

Similar preparations suitably perfumed form Toilet Lanolin and Lanolin Cream.

**Cholesterol.** *Syn.* CHOLESTERIN.  $C_{27}H_{45}OH$ ,  $H_2O = 404.4$ .

Cholesterol is a constituent of all animal cells and therefore occurs in most foods, egg yolk being especially rich. It is more commonly familiar as a constituent of gall-stones, which often contain it to the extent of 90% or more, and from which it may be obtained by extraction with spirit. It is usually obtained from wool-fat by saponification with potassium hydroxide and extraction with ether. It occurs as a white, odourless, crystalline compound, m.p. about  $145^{\circ}$ .

**Soluble** in acetone, chloroform, ether and hot alcohol; sparingly soluble in cold alcohol; slightly soluble in water. Soft paraffin mixed with  $\frac{1}{2}$  to 1% will take up 10 to 20% of water.

**Uses.** Cholesterol has the property of neutralising many hæmolytic poisons such as snake-venoms, saponins, etc., and for this reason has been used in the treatment of various hæmolytic diseases such as hæmoglobinuria, pernicious anæmia, etc., but without any marked success. It has also been advocated for use in tuberculosis. A spirituous lotion,  $\frac{1}{2}$  to  $\frac{1}{2}\%$ , has been used as a

stimulating application, and it is incorporated in many cosmetic ointments as a "skin food."

**Camphosterin** (*Richter, London*). Cholesterin 0.05 g., camphor 0.20 g., guaiacol 0.05 g., quinine 0.05 g., olive oil to 2 ml. *Dose*.—2 ml. intramuscularly on alternate days for a course of 20 injections. In pulmonary tuberculosis.

**Oxycholesterol**.  $C_{27}H_{48}O_2$ . A white unctuous substance, m.p. about 40°. Readily takes up water (up to 500%) forming water-in-oil emulsions. Is used in toilet creams.

**Adeps** (*B.P., U.S.P. XI*). *Syn.* ADEPS PRÆPARATUS, ADEPS SUILLUS (*P. Helv. V*), AXUNGIA (*P. Ned. V*), ADEPS LOTUS (*P. Dan.*).

The purified fat of the hog, *Sus scrofa* (Linn.)—from the "flare" or "omentum" which also contains 60% triolein, sold when separated by freezing and pressure as "Lard Oil" (**Oleum Adipis**), a colourless or pale yellow oil with peculiar odour. The remainder is palmitin and stearin. **Soluble** 1 in 22 of ether, hardly soluble in alcohol. **Adeps Induratus** is for use in the tropics. The liquid constituent is removed to a great extent by pressure.

Hydrogenated palm kernel oil, m.p. 40° to 42°, is a suitable fat to replace lard and suet ointments in tropical countries.—A. F. Caldwell, *Quart. J. Pharm.*, 1939, 697.

**Adeps Benzoinatus** (*B.P.*). *Syn.* ADEPS BENZOATUS (*P. Dan., P. Jap. V*), ADEPS SUILLUS BENZOINATUS (*Fr. Cx.*).

Is made with 3% Sumatra benzoin. To be avoided as a basis for eye ointments.

Experiments on the keeping properties of benzoinated lard have shown that 1 to 2% of Siam benzoin is more satisfactory than 3% of Sumatra benzoin.

In many ointments lard and benzoinated lard have been replaced by a mixture of wool fat and hard and soft paraffins. A mixture of the same composition as Unguentum Simplex, *B.P.* 1932, was included as a War Emergency preparation in the Codex Addendum 1918, under the name of Adeps Factitius, and was widely used as a substitute for lard in preparing *B.P.* and *B.P.C.* ointments. The Second Addendum to the *B.P.* 1932 includes alternative formulæ for official ointments for which lard was formerly required, and in a similar manner many other ointments may with advantage be prepared with simple ointment instead of lard or benzoinated lard.

**Adeps Benzoinatus** (*U.S.P. XI*) is made with 1% of Siam benzoin, and 5% or more of lard may be replaced by white wax in southern latitudes or in the warm season in other parts.

**Sevum** (*B.P., U.S.P. XI, P. Helv. V*). *Syn.* SEVUM PRÆPARATUM, SEBUM OVILLUM DEPURATUM (*Fr. Cx.*).

The purified internal fat of the abdomen of the sheep, prepared by cutting up the fresh omentum, melting and straining. M.p. 45° to 50°.

**Soluble** 1 in 60 of ether and 1 in 45 of boiling alcohol 90%.

**TROPHIC ULCERS.** The following treatment was found successful in trophic ulcers in leprotic patients which have failed to respond to all other treatments. After removal of carious bone and dead skin and general cleaning up of the ulcer, an ointment is prepared consisting of beef suet, 2 parts; ghee, 1 part;

beeswax,  $\frac{1}{2}$  part. The ointment is melted and the mixture poured into the clean ulcer. As the ointment congeals a piece of thick white material is placed over the ulcer and a bandage sewn on. The ointment and dressing are at first changed twice weekly and then once a week.—N. H. Maynard, *Leprosy Rev.*, 1939, 118.

**Sevum Benzoïnatum** (B.P.C., P. Helv. V). *Syn.* SEVUM BENZOATUM. Suet digested with 3% of benzoïn.

**Sevum Phosphoratum** (B.P.C.). Contains 10% of phosphorus.

**"University Cream."** *Syn.* EMULSIO SEVI (formerly in U.C.H.). Beef suet 40 ozs., arachis oil 5 ozs., syrup 25 ozs., benzoic acid 40 grains, decoction of Irish moss 70 ozs., water to 1 gallon. Melt the suet, add the oil and the benzoic acid. Heat the moss decoction to about 60°, place in an emulsifier and add the fats at about the same temperature. Finally add the syrup and water. This keeps well and mixes well with milk. For use instead of cows' cream in preparing infants' feeds.

**New Zealand Cream** (*Mothercraft Training Society, London*), as manufactured in New Zealand's Government factory, contains 50% fat, of which  $\frac{1}{2}$  is animal oil, including fresh New Zealand butter and cod-liver oil, and  $\frac{1}{2}$  vegetable oils, mainly pea-nut; sugars, mainly dextrose and a little lactose, make up 40%. Satisfactory in use, readily assimilable, sterile, containing vitamins intact, and high calorific value of 180 per ounce.

## ADRENALINA

B.P., Fr. Cx., P. Ital. V, etc.



*Syn. and Prop. Names.* ADRENALIN, HEMISINE, SUPRARENALIN (*Armour, London*), ADRENINE, RENAGLANDIN (*Oppenheimer, London*), SUPRARENIN (P. G. VI), TAKAMINA (F.E. VIII), ADNEPHRIN, VASO-CONSTRICTINE (*Duncan, Flockhart, Edinburgh*), LEVORENINUM (P. Belg. IV), EPINEPHRINA (U.S.P. XI), o-DIOXYPHENYLETHANOLMETHYLAMINE, l- $\alpha$ -3 : 4-DIHYDROXYPHENYL- $\beta$ -METHYLAMINOETHANOL.

[P1] "*Suprarenal gland, the active principles of; their salts.*"

[S6] "*Suprarenal gland, the active principles of, their salts—specify proportion in a preparation either*

- (a) *as the proportion of suprarenal gland or of the cortex or of the medulla of the gland, as the case may be, contained in the preparation; or*
- (b) *as the amount of suprarenal gland, or of the cortex or of the medulla of the gland, as the case may be, from which a specified quantity of the preparation was obtained, together with an indication whether the amount relates to fresh or to dried gland substance.*"

*Dose.*—By injection,  $\frac{1}{1000}$  to  $\frac{1}{100}$  grain (0.0001 to 0.0005 g.).

U.S.P. XI average dose  $\frac{1}{100}$  grain. Fr. Cx. single dose 0.001 g., max. in 24 hours 0.02 g.

It is an active principle of the suprarenal gland and may be obtained from the glands or prepared synthetically (*vide infra*). It occurs as a white or pale buff-coloured crystalline powder.

**Soluble** sparingly in water, readily in mineral acids and boric acid solution forming corresponding salts, also in solutions of sodium or potassium hydroxide. Aqueous solutions of its salts are laevorotatory. **Insoluble** in alcohol, ether, chloroform, light petroleum, liquid paraffin and other organic solvents. Oleic acid is a poor solvent. Not precipitated by ordinary alkaloidal reagents. It is chemically a powerful reducing agent.

**Incompatible** with oxidising agents, alkalis, gum and tannin.

**Manufacture.** The suprarenal glands are reduced to pulp and macerated, excluding oxygen as much as possible, in warm (50° to 80°) water or very dilute acid for 5 hours, the mixture being then heated at 90° to 95° to coagulate albuminoids. This aqueous extractive is evaporated and extracted with alcohol. Precipitation from this liquid of impure adrenaline follows by means of ammonia. It is purified by ether-alcohol, and reprecipitation with ammonia or fixed alkali.

Synthetic adrenaline may be obtained by the interaction of catechol and chloroacetyl chloride to give chloroacetylcatechol, which is treated with methylamine and the product reduced to give racemic adrenaline. The *laevo* compound is separated by fractional crystallisation of the *d*-tartrates. *d*-Adrenaline has only about one-fifteenth the activity of the *l*-compound and the racemic form has therefore only about one-half the activity of *l*-adrenaline.

[P] **Liquor Adrenalinae Hydrochloridi (B.P.).**

**Dose.**—By subcutaneous injection, 2 to 8 minims (0.12 to 0.5 ml.). The B.P. has no dose for oral administration, but doses of 10 to 30 minims (0.6 to 2 ml.) are often given. As a spray the solution is diluted to 1 in 2500, or even 1 in 5000 is effective in the nostrils or within the uterus.

Adrenaline 1, chlorbutol 5, sodium chloride 9, dilute hydrochloric acid 3, water to 1000.

The solution is liable to become pink in colour on exposure, and the Committee on Pharmacy and Pharmacognosy of the Pharmacopœia Commission (*Report* 13) have recommended the addition of 0.05% of sodium metabisulphite to retard the development of this colour.

Adrenaline, when in solution with certain of the silver compounds, is inactivated in a few hours, and when such a solution is required it is advisable to use a fresh mixture.

[P] **Liquor Epinephrinae Hydrochloridi (U.S.P. XI).**

**Average Dose.**—8 minims (0.5 ml.) by parental injection.

A physiologically standardised solution of adrenaline hydrochloride in water and hydrochloric acid of the same strength as Liquor Adrenalinae Hydrochloridi (B.P.). Not more than 0.5% of chlorbutol or other suitable preservative may be added, but the nature and amount of the preservative must be stated on the label.

[P] **Soluté d'Adrénaline (Fr. Cx.)** is similar to B.P., but contains sodium sulphite 0.08%, instead of chlorbutol. **Dose.**—1 g.

[P] **Oleum cum Adrenalina (Fr. Cx.).** Contains adrenaline 0.1%, in alcoholic hydrochloric acid, mixed with a solution of chlorbutol in castor oil, and adjusted with olive oil.

The addition of 0.15% of sodium acid phosphate as a preservative is suggested. —J. Rae, *Pharm. J.*, i/1936, 446.

Solution of adrenaline hydrochloride retains its full potency for 16 months when stored under carbon dioxide at laboratory temperature, and while 0.1% of sodium metabisulphite has little influence on the maintenance or loss of potency under these conditions, it does improve the keeping quality of the solution. The colour of solution of adrenaline hydrochloride is not an indication of its potency, clear, colourless solutions having been shown to have lost 50%

of their activity, whilst coloured solutions may retain their full potency.—H. R. Rowlinson and S. W. Underhill, *Quart. J. Pharm.*, 1939, 392.

**Toxic Effects and Contraindications.** Some people show toxic effects, e.g., anxiety, palpitation, rapid pulse, tremors, dizziness, coldness of the extremities, etc., with even small doses of adrenaline, especially when given simultaneously with certain local anæsthetics such as procaine hydrochloride or cocaine. This hypersusceptibility occurs especially in patients of nervous temperament, and most markedly in those with toxic goitre, in whom its use is best avoided. Its use is also contraindicated in diabetic patients, since it raises the blood sugar by mobilising the glycogen of the liver.

Owing to its action on the heart, it should be used only with great caution in patients with cardiac disease, and it should never be given to a patient under chloroform anæsthesia, since this may precipitate ventricular fibrillation.

On the basis of animal experiments it has been suggested that continued use of adrenaline injections may give rise to arteriosclerosis, but there is little clinical evidence in support of this.

Although the ischæmic action of adrenaline is a valuable aid to the ophthalmic surgeon, its use in any visual affection following a severe hæmorrhage may be harmful owing to its constricting action on the retinal vessels.

Tetany following the use of cocaine and adrenaline (1 in 1000) is of fairly frequent occurrence. It is not a drug intoxication, but is due to a combination of hypoparathyroidism, hyperventilation, and adrenaline in nervous patients. Quickly relieved by parathyroid extract subcutaneously.—S. E. Roberts, *J. Amer. med. Ass.*, ii/1929, 906.

Latent and finally active tetany in a patient who received adrenaline during asthmatic attacks is considered to be the result of an alkalosis due to hyperventilation. Tetany did not appear when codeine was given in place of adrenaline.—Ellsworth and Sherman, *J. Amer. med. Ass.*, i/1936, 284.

**Uses.** When applied locally adrenaline causes constriction of blood vessels and blanching of the skin and mucous membrane, and is added to local anæsthetics to retard diffusion and produce ischæmia. This local constricting effect lasts from  $\frac{1}{2}$  to 2 hours. It is useful for checking capillary bleeding, epistaxis and menorrhagia, the bleeding after tooth extractions, from superficial wounds and abrasions, and during operations to check hæmorrhage and blanch the parts, especially for operations on the eye, ear, nose, throat or larynx. Adrenaline may also be employed, in the form of suppositories or ointment, for its constrictive action in hæmorrhoids and other inflammatory conditions of the anus and rectum. Solutions of from 1 in 10,000 to 1 in 5000 are useful for application in the form of a spray to the nasal mucous membrane in coryza, asthma and hay fever. It has also been used in 1% and 10% solution as a very fine throat spray in asthma.

Hypodermic injections are used to relieve asthmatic spasms, to control anaphylaxis from serum injection and to reduce the swelling in giant urticaria. Hypodermic injection does not materially raise blood pressure, as the local vascular constriction prevents absorption. Generally speaking, intravenously its use is dangerous and



should be avoided except in emergencies, though good results are claimed in the treatment of chronic malaria by repeated intravenous injections of 0.01 to 0.1 mg. (Ascoli's method).

It may be given by mouth to check hæmorrhage from the stomach, or may be injected into the rectum, bladder and uterus for bleeding. It is of no value in hæmoptysis, and of little use in remote hæmorrhage however given, in fact the rise in blood pressure may increase the hæmorrhage.

**INTRACARDIAC INJECTION IN RESUSCITATION.** Adrenaline has been given by direct injection into the heart to revive its action when in sudden failure. It is not necessary or advisable to give more than 1 ml. of the 1 : 1000 solution, in view of the possible danger of a tetanic contraction of the muscle with systolic stoppage of the heart. The injection should be given directly into the cavity of the heart and not into its walls. Injection into the right auricle is probably the ideal procedure, but the right ventricle may also be used.

For resuscitation in cardiac arrest, artificial respiration should be resorted to first by the usual methods. If at the end of 3 or 4 minutes no pulse can be felt, and especially if no heart-beats can be heard on auscultation, adrenaline should be given by intracardiac injection and artificial respiration continued for a minute or two. If the heart still does not beat cardiac massage should be employed without further delay.

#### References to Clinical Use of Adrenaline.

**ASTHMA.** In status asthmaticus the continuous injection of adrenaline in small quantities, up to even a drachm in  $\frac{1}{2}$  hour, the only cure.—A. F. Hurst, *Brit. med. J.*, ii/1929, 297.

Status asthmaticus can always be arrested by the continuous method of injecting adrenaline. The needle is kept in position, and with a full syringe and after an initial injection of a dose known to cause no unpleasant symptoms, one or more minims is injected every 15, 30 or 60 seconds (according to the patient's reaction), the rate being varied until it is found how frequently a dose can be given without causing unpleasant symptoms. The injections are continued if necessary for 30 minutes or more. Relief always follows and generally the patient falls into a deep sleep.—A. F. Hurst, *Pharm. J.*, ii/1934, 705.

The predisposing cause of asthma is a low content of adrenaline in the blood; patients with asthma become unable to dilate the bronchiolar airway when chronic infections cause a constriction.—J. H. Burn, *Proc. R. Soc. Med.*, 1933, 31.

Better results are obtained by inhalation (of 1% solution) than by injection. The effect is more rapid and side-effects are rare.—J. B. Graeser and A. H. Rowe, *J. Lab. clin. Med.*, 1936, 1134.

**HÆMOPYSIS.** Adrenaline cannot be justified on experimental grounds, but given intratracheally over back of the tongue said to be effective (1 ml. of 1 in 1000 solution in 2 ml. of water.—*Münch. med. Wschr.*, Feb., 1928), but this cannot be done in an emergency when blood is welling up into the mouth. Semi-sitting posture best.—F. G. Chandler, *Lancet*, i/1930, 589.

**HEADACHE.** Headache due to obstruction of frontal sinuses. Adrenaline hydrochloride solution 1 in 4000, 1 dr., and saturated boric acid solution 1 dr. used in an atomiser four times daily gives relief.—E. Podolsky, *Int. J. Med.*, July, 1930.

**HEART BLOCK.** Twelve cases of complete heart block tested with adrenaline chloride. The response of the heart is determined not by the amount of the dose but by the rate of the heart at the time of injection. High initial rates are followed by little or no gain in rate, but slow initial rates are followed by pronounced acceleration. For a given initial rate 0.25 ml. of adrenaline chloride solution

produced as much acceleration as a dose four times as large.—A. R. Gilchrist, *Quart. J. Med.*, Oct., 1933, 483.

Rheumatic heart block well treated with adrenaline solution, 4 m. hypodermically—a total of 32 m. in 5 days.—G. A. Sutherland, *Prescriber*, 1926, 199.

**MALARIA.** Good results in chronic malaria, with splenomegaly, anæmia and cachexia, obtained from the use of daily intravenous injections beginning with  $\frac{1}{100}$  mg. and increasing by  $\frac{1}{100}$  mg. daily to a dose of  $\frac{1}{10}$  mg. Resistance to quinine often disappears, and the quinine dosage can be lowered when adrenaline is employed. The adrenaline is stated to act by sterilising the spleen and making relapses through further protozoal invasion impossible. Of 15 patients treated two years ago and 20 one year ago none have shown enlargement of the spleen again, and none have relapsed.—M. Ascoli, *Munch. med. Wschr.*, 1937, 370.

Six cases treated by the intravenous injection of adrenaline (Ascoli's method) with excellent results. The adrenaline was given in doses of 0.01 to 0.1 mg. every day for 20 days.—G. Pomilia, per *Trop. Dis. Bull.*, 1937, 598.

Numerous references to excellent results from the use of adrenaline intravenously in acute and chronic malaria and in malarial splenomegaly.—*Trop. Dis. Bull.*, 1937, 617-619; 1938, 565; 1939, 685.

Care must be taken that the adrenaline is of the best quality and the solution freshly prepared. It is claimed that the first injection is followed quickly by a diminution of fever, a normal blood picture, a feeling of better health, and a decrease in the size of the spleen, and the full course of injections will prevent relapse for about a year.—Per *Lancet*, ii/1939, 942.

**MIGRAINE.** Adrenaline subcutaneously aborts migraine attacks in a high proportion of cases.—T. C. Hunt, *Lancet*, ii/1933, 285.

**SERUM SICKNESS.** Recovery in a case of severe serum shock in a girl of 8 years, which developed three minutes after intramuscular injection of 5 ml. of concentrated scarlet fever antitoxin; treated by artificial respiration and hypodermic injection of adrenaline hydrochloride solution.—J. Grant and M. M. Scott, *Lancet*, ii/1934, 80.

**STOKES-ADAMS ATTACKS** have been well treated with adrenaline solution (5 m. doses) subcutaneously.

**VOMITING IN MALARIA** has been well treated with 7 to 8 minims—one dose sufficient.

**X-RAY SICKNESS.** A method for controlling this condition far superior to all others is the administration by the mouth of 10 minims of Liq. Adrenalin. Hydrochlor. as frequently as necessary up to 6 doses or even more, in the 24 hours.—N. S. Finzi, *Brit. med. J.*, ii/1935, 1072.

**[D-P1-81] Adrenaline Catheter Lubricant.** Adrenaline (base) 1, cocaine 10, atropine 10. Dissolve the adrenaline in hydrochloric acid *q.s.* (0.6 is usually sufficient) diluted with dehydrated alcohol 30. Dissolve the alkaloidal bases in oleic acid 20 and mix this and the adrenaline solution with sufficient castor oil and dehydrated alcohol in proportion of 4 to 1 to make 1000 of the lubricant.

**[P1] Guttæ Adrenalinæ cum Acid. Boric. (R.L.O.H.).**

Solution of adrenaline hydrochloride 1 dr., boric acid 10 gr., sterile water to 1 oz.

**[P1] Guttæ Zinc. Sulph. cum Adrenalin. (R.L.O.H.).**

Solution of adrenaline hydrochloride 1 dr., zinc sulphate  $\frac{1}{2}$ , 1 or 2 gr., boric acid 10 gr. sterile water to 1 oz.

**[P1] Insufflatio Adrenalinæ (B.P.C.). Syn. ADRENALINE SNUFF.** Adrenaline, about 1 in 1300, with boric acid, camphor, menthol, potassium chlorate, oil of eucalyptus and lycopodium.

**[P1] Nebula Adrenalinæ Aromatica (B.P.C.). Syn. ADRENALINE INHALANT.**

Adrenaline, 1 in 1000, eucalyptol and oil of sweet birch in an oily base.

**[P1] Neb. Adrenal. (N.I.F.).** Solution of adrenaline hydrochloride 45 m., sodium chloride 4 gr., water to 1 oz.

**Strong Solution for Use in Asthma.** Adrenaline 1 g., chlorbutol 0.09 g., 2N hydrochloric acid 2.8 ml., sodium bisulphite 0.01 g., water to 10 ml. Inhalation takes place through the mouth, the ball of the spray being pressed once at

the beginning of every inspiration and the patient breathes deeply with the mouth wide open. The dose of adrenaline is of the order of  $\frac{1}{16}$  mg.—N. A. Nielsen, *Lancet*, ii/1936, 848.

[P1] **Neb. Adrenal. c. Benzamin. Hydrochlor.** (*N.I.F.*).

Solution of adrenaline hydrochloride  $1\frac{1}{2}$  dr., benzamine hydrochloride 5 gr., glycerin 40 m., distilled water to 1 oz.

[D-P1-81] **Nebula Adrenalinae et Cocaina** (*B.P.C.*).

Adrenaline 1 in 5000, and cocaine hydrochloride 1% with chlorbutol and sodium chloride in water.

[P1] **Solutio Adrenalini Composita** (*St. T. H.*).

Solution of adrenaline hydrochloride 5 m., atropine sulphate  $\frac{3}{16}$  gr., strychnine hydrochloride  $\frac{1}{16}$  gr., distilled water to 10 m.

[P1] **Suppositorium Adrenalinae** (*B.P.C.*) contains  $\frac{1}{16}$  gr. of adrenaline.

[D-P1-81] **Suppositorium Adrenalinae et Cocaina** (*B.P.C.*) contains  $\frac{1}{16}$  gr. of adrenaline and  $\frac{1}{2}$  gr. of cocaine hydrochloride.

[P1] **Unguentum Adrenalinae** (*B.P.C.*). Adrenaline 0.1% in a hydrous wool fat and white soft paraffin basis.

[D-P1-81] **Unguentum Adrenalinae et Cocaina** (*B.P.C.*) is the same with addition of 1% of cocaine hydrochloride.

[P1] **Adrenalin Inhalant** (*Parke, Davis, London*). A 1 in 1000 solution of adrenaline with 3% of chlorotone in an aromatised oil. Soothing and astringent in inflammatory affections.

[P1] **Adrenutol** (*Evans, Sons, Lescher & Webb, Liverpool*). A solution containing adrenaline 2 mg., chlorbutol 2 mg., glycerin 0.7 ml. and distilled water to 1 ml., for the treatment of asthma and other allergic disorders by subcutaneous or intramuscular injection.

[P1-87] **Asthmolylin** (*C. Zimmerman, London*). Solution of suprarenal and pituitary glands for subcutaneous injection in asthma.

[P1-87] **Evatmine** (*British Organotherapy Co., London*). Adrenaline (8 m. of 1 in 1000 solution) and pituitary (whole gland) extract in 1 ml. ampoules for subcutaneous injection in the treatment of asthma.

**Glaucozan** (*Saccharin Corporation, London*). Solution containing 0.2% of synthetic *d*-adrenaline and 1% of methylaminoacetocatechol (adrenalone). Given by subconjunctival injection in the treatment of glaucoma.

[P1] **Laevo-Glaucozan** (*Saccharin Corporation, London*). A solution containing 2% each of synthetic *l*-adrenaline and methylaminoacetocatechol (adrenalone). A powerful mydriatic for instillation, following the use of a local anæsthetic in the treatment of chronic glaucoma. The preparation must not be injected in any manner.

[P1-87] **Infundrenalin** (*Evans, Sons, Lescher & Webb, Liverpool*). Infundibulin 0.5 ml., adrenaline (1 in 1500) 0.5 ml. (in two separate ampoules). In bronchial asthma and hay fever.

[P1-87] **Pitrenalin** (*Parke, Davis, London*). Pituitrin and adrenaline hydrochloride solution in twin ampoules producing, when mixed, a solution containing 5 i.u. of pituitary (posterior lobe) extract and 6 m. of adrenaline hydrochloride solution in normal saline to 1 ml. *Dose*.— $\frac{1}{4}$  to 1 ml. hypodermically.

[P1-87] **Riddobron** (*Riddell Products, London*). A solution containing papaverine, hyoscine, atropine methylnitrate, adrenaline, pituitary extract and nitrates for use as a spray in asthma and hay fever.

(A foreign proprietary of similar composition was formerly marketed in this country under the Registered Trade Name "Bronchovydrin.")

[P1] **Vernol Ointment** (*Allen & Hanburys, London*). Contains adrenaline 1 in 5000 with anæsthesine 1 in 40. Soothing and astringent for catarrhal conditions of the nasal mucous membrane.

#### SOME COMPOUNDS RELATED TO ADRENALINE

**Epine** (*Burroughs Wellcome, London*). 3:4-Dihydroxyphenylethyl-methylamine.  $C_8H_{11}(OH)_2 \cdot CH_2 \cdot CH_2 \cdot NH \cdot CH_3 = 167.1$ .

A 1 in 100 solution equals a 1 in 1000 solution of adrenaline. Solutions acidified by the addition of 0.5 ml. of sulphurous acid to 100 ml. are more stable than adrenaline solutions.

It is supplied in 1% solution to be diluted with normal saline. It resembles adrenaline in action, but the rise of blood pressure though not so intense is said to be more prolonged. For use in ophthalmic work 0.1%; as a styptic to bleeding surfaces 0.01 to 1%; and hypodermically 1% solutions are used. For intravenous use 1 ml. of 1% solution is diluted with 500 ml. of normal saline.

**Paredrine** (*Smith, Kline & French, Philadelphia*). *p*-Hydroxy- $\alpha$ -methylphenylethylamine hydrobromide. Has a powerful pressor action due to stimulation of the smooth muscle of the arterial wall and is effective when given by mouth, intramuscularly or intravenously. Good pressor effects with 20 or 30 mg. orally, 10 or 20 mg. intramuscularly, and 5 or 10 mg. intravenously.

It possesses about  $\frac{1}{10}$  the pressor activity of adrenaline when given subcutaneously and twice that of ephedrine on oral administration. Its chief clinical effects are raising of the blood pressure, dilatation of the pupil and constriction of the blood vessels of the nasal mucosa. No appreciable effect is produced on the central nervous system and in reasonable doses it has no effect on asthma. —Abbot and Henry, *Amer. J. med. Sci.*, 1937, 193, 681.

Paredrine is useful in raising the blood pressure to satisfactory levels if it becomes unduly lowered by spinal anaesthesia; it has little or no direct effect on the heart, its direct action being apparently limited to the peripheral vessels. No untoward effects have been noted following its administration. The procedure adopted is as follows: when the systolic pressure falls markedly, but not below 50, 10 mg. is given intramuscularly. If no rise occurs within 5 minutes a second injection of 10 mg. is given intramuscularly. If the systolic pressure falls below 50, 5 mg. is given intravenously. When the systolic pressure has again fallen below 100, usually in 15 or 20 minutes after intravenous injection, 10 mg. is given intramuscularly. —M. D. Altschule and S. Gilman, *New Engl. J. Med.*, ii/1939, 500.

**Stryphnon** (*Camden Chemical Co., London*). Preparations of methylaminocatechopyrocatechin for use as a hæmostatic, available as the solution (5%), suppositories (3%), injection (subcutaneous 0.5%, intravenous 0.05%) and in other forms.

**Pholedrine**. *Prop. Name*. VERITOL (*Knoll, London*). (Tablets, 0.05 g., solution, 3%, and ampoules, 1.1 ml. of 2% solution).

*Dose*.—(As a circulatory tonic) 10 to 20 drops or  $\frac{1}{2}$  to  $\frac{1}{4}$  tablet several times daily, or  $\frac{1}{2}$  ampoule intramuscularly or subcutaneously, or  $\frac{1}{2}$  ampoule intravenously. (As a restorative in collapse)  $\frac{1}{2}$  to 1 ampoule intravenously hourly if necessary, or 1 ampoule intramuscularly or subcutaneously.

$\beta$ -(4-Hydroxyphenyl)-isopropylmethylamine, a circulatory stimulant and restorative, having a less rapid but more prolonged action than adrenaline, and without the cardiac effects of ephedrine.

In hypotension and collapse, poisoning by carbon monoxide, hypnotics, etc., in infectious diseases such as pneumonia, diphtheria, etc., in surgical and traumatic shock, and for pre- and post-operative treatment of the circulation.

Its action lies between that of adrenaline and ephedrine; it resembles adrenaline in its low toxicity and absence of toxic effects on the heart and ephedrine in its long continued action and activity after oral administration. In the healthy human subject 10 mg. injected intravenously raised the blood pressure for 10 to 15 minutes; after intramuscular injection the rise persisted for 40 to 60 minutes; the effect of 40 to 80 mg. taken by mouth lasted for 2 hours. It is reported that blood-pressure levels of 200 mm. can be attained in this way. The most convincing objective evidence of efficiency is the rapid and sustained rise of blood-pressure which takes place in collapse and shock. In its effect on respiration it does not appear to be comparable with such substances as Coramine and Cardiazol. The main indication for the drug in the surgical field is the treatment of failure of the peripheral circulation during and after an operation. It has also been used successfully in broncho-pneumonia in children (given by the mouth alternately with Cardiazol) and in the acute heart failure of toxic diphtheria. —*Lancet*, ii/1938, 1070.

Clinically it has been found of considerable value in the prevention or control of surgical shock. Oral administration is not advised as the effects are inconstant. After intravenous injection the effects come on very rapidly, but sometimes pass off in about a quarter of an hour. Intramuscular injection produces a slower but more prolonged effect. With ordinary doses, 20 mg., the blood pressure is not much raised in the normal, but good effects are produced where the blood pressure is low. —R. St. A. Heathcote, *Med. Annu.*, 1939, 380.

Of all the drugs so far tried it is the most satisfactory for raising the blood pressure. The dose for intramuscular injection is 0.75 to 1 ml.; nothing less than 0.75 ml. is effective with a low blood pressure. The blood pressure begins to rise in 3 to 5 minutes and progresses to a maximum in about 20 minutes, usually reaching the normal systolic figure. The fall from this level mostly takes place during the succeeding 20 to 40 minutes, when, if the operation is still proceeding, a further dose of the same amount may be considered necessary. Subsequent injections continue to be effective, although in a truly shocked patient 1.5 ml. is usually needed. Veritol given intravenously acts immediately, and according to the dose raises blood pressure to the normal systolic level or considerably higher. It has been found by experience that 0.25 ml. is the useful dose during operation; the effect is probably over in 20 to 25 minutes. Combined intramuscular (0.75 ml.) and intravenous (0.25 ml.) injections will restore the blood pressure almost immediately and maintain it for 30 to 45 minutes. It may also be given with advantage to debilitated patients for a few days after major operations (0.75 to 1 ml. intramuscularly) when a steady rise lasting 40 to 60 minutes follows, with a general improvement and feeling of well-being. No unpleasant effects have been noted.—H. Dodd, *Lancet*, i/1940, 360.

The pharmacological actions and therapeutic uses of some compounds related to adrenaline.—J. A. Gunn, *Brit. med. J.*, ii/1939, 155, 214.

### [P1] Suprarenal (or Adrenal) Gland.

Small, flattened, yellowish bodies—one at the upper end of each kidney. In man each gland weighs about 4 grammes. Each suprarenal gland is enclosed in a fibrous capsule and is composed of two parts, a cortex and a medulla. The cortex contains a glandular epithelium embedded in a fine network of connective tissue; the medulla contains finely granular chromophil cells permeated by large venous sinusoids.

[P1] **Suprarenalum** (*B.P.C.*). *Syn.* POUDRE DE GLANDE SUPRÉNALE (*Fr. Cx.*).

*Dose.*—1 to 5 grains (0.06 to 0.3 g.) three times a day.

The cleaned, dried and powdered suprarenal glands of oxen or other mammals. An average sheep's gland weighs about 30 grains (2 g.) and yields about 5 grains of dry powder.

By glycerin extraction of adrenal glands a pressor principle effective orally can be obtained. It is believed to differ from adrenaline.—Hoskins and Gottlieb, *Endocrinology*, 1936, 20, 188.

*Uses.* Originally the fresh glands were used in the treatment of Addison's disease, later the dried glands were used, also liquid extracts and, lastly, an extract prepared from the cortex of this gland is now used in this disease. The active principle of the medulla is adrenaline (*vide antea*). The whole gland has also been used in the treatment of Graves' disease.

Raw adrenal gland of value in post-influenzal debility— $\frac{1}{2}$  gland thrice daily on an empty stomach. Also of value in preventing attacks of asthma.—L. J. Picton, *Brit. med. J.*, i/1927, 641.

### [P1] Suprarenal Snuff.

Dry suprarenal gland 1, menthol 2, ammonium chloride 6, boric acid 4, lycopodium 4; for use in hay fever.

[P1] **Adreno-Cortin** (*Endocrines-Spicer, Watford*). Capsules of adrenal cortex extract, each containing 5 m. In Addison's disease and in less severe fatigue syndromes, including those due to infectious diseases. *Dose.*—1 to 2 twice or thrice daily.

[P1-87] **Adreno-Spermin** (*Endocrines-Spicer, Watford*). Tablets contain total adrenal, thyroid, spermin extract (from gonads), and Calcium Phosphorus Co. Asthenic conditions.

[P1] **Extractum Suprarenali Corticis (B.P.C.).** *Syn.* CORTIN.

*Dose.*— $1\frac{1}{2}$  to  $2\frac{1}{2}$  drachms (5 to 10 ml.).

An aqueous solution of the active principle, or principles, of suprarenal cortex obtained by extraction with alcohol and subsequent purification with benzene, acetone and light petroleum.

*Glycerin Extract for Oral Administration.* Fresh, ground beef cortex was extracted with an equal volume of glycerin at  $4^{\circ}$  for several days. An equal volume of alcohol was then added, the product filtered through crystallite to remove adrenaline and the alcohol removed from the filtrate *in vacuo*. 1 ml. of glycerol extract represented about 1.5 g. of fresh cortex and it contained from 1:10,000 to 1:50,000 of adrenaline. It was employed in Addison's disease, usually in doses of 2 to 4 ml. three times daily after food, but up to 20 ml. per day was tried. Results in early cases were completely satisfactory, provided treatment was continuous and all stresses avoided. In severe cases the extract sufficed only under the most favourable circumstances and in the absence of strenuous activity.—F. A. Hartman, G. W. Thorn and R. R. Durant, *Endocrinology*, 1937, 516.

**PHYSIOLOGY.** The cortex of the suprarenal gland is essential to life, although the medulla may be removed without causing death, providing the cortex is undamaged. Extracts of the cortex when injected relieve the symptoms of Addison's disease, and up to the isolation of the crystalline principles of the gland was used mainly for this purpose. Death following removal of the suprarenal cortex is considered to be due to circulatory collapse resulting from insufficient circulating fluid, the volume of which is controlled by the suprarenal cortex. Hence the value of extracts of the cortex or preparations of the cortical hormones in the treatment of traumatic shock.

The relationship of the suprarenal cortex to sodium and chloride metabolism has been much discussed. It appears that early in the course of adrenal insufficiency the rate of sodium excretion through the kidney increases and the concentration of sodium ions in the blood decreases. There is also a decrease of chloride or of bicarbonate or of both. The loss of sodium from the body is accompanied by a loss of water which leads to decreased blood volume and a state of shock, and to a rise in serum potassium.

Ascorbic acid occurs in the suprarenal gland. It is present in considerable quantities in the cortex and to a less degree in the medulla. Whether the gland merely serves as a reserve storage organ or requires the vitamin for its own normal functioning is still a matter of controversy.

**Uses.** Suprarenal cortex extract is employed in the treatment of Addison's disease, though it has now been replaced to some extent by desoxycorticosterone acetate. It has also been used in neurasthenia, traumatic shock, the acute toxæmia of burns, Paget's disease, and in the persistent vomiting of pregnancy.

(For use of sodium chloride in Addison's disease, *see under* Sodii Chloridum.)

**ADDISON'S DISEASE.** Chief value of cortical extract in Addison's disease is in treatment of the relapse; the extract has no definite effect on hypotension or pigmentation.—G. A. Harrop *et al.*, *Amer. med. Ass.*, i/1933, 1850.

Cortical extract in adequate dosage, by itself or in addition to salt therapy, gives a much better clinical response than salt alone. When the dose of cortical

extract is adequate the addition of salt is of no benefit, but when it is inadequate the addition of salt may help appreciably. When patients have gone into a crisis in spite of having large doses of salt, the administration of cortical extract has produced recovery.—S. L. Simpson, *Proc. R. Soc. Med.*, 1936, 29, 1143.

Nine cases of Addison's disease were treated. Four deaths occurred, one from auricular fibrillation while the Addison's disease was in remission, and three from the disease itself. The remaining five have responded well to the treatment; they have survived for periods from 19 to 37 months at the date of the report and were then receiving maintenance doses of sodium chloride only (7.5 to 15 g. per day) without cortical extract, and were showing steady improvement. Very large doses of cortical extract (up to 40 or 50 ml. daily) were required in some of the cases in the initial stages.—J. F. Wilkinson (*Report to Therapeutic Trials Committee*), *Lancet*, ii/1937, 61.

**BURNS, ACUTE TOXÆMIA OF.** In severe toxæmia death within 100 hours is the usual outcome, whatever the treatment, but three such cases in which a fatal outcome was to be expected recovered following the use, as an adjuvant measure, of extract of suprarenal cortex (Eucortone). A dose of 1 ml. subcutaneously every two hours from the onset of acute toxæmia will suffice for a child, and 2 ml. or more every hour for an adult; injections should be continued till 100 hours after injury and renewed if toxic manifestations reappear. It should only be considered, however, as an adjuvant measure.—W. C. Wilson, G. D. Rowley, and N. A. Gray, *Lancet*, i/1935, 1400.

**CONFUSIONAL STATES.** Five cases of acute confusion developing during typhoid fever were successfully treated with suprarenal cortical extract 2 ml. with vitamin C daily intravenously. Four cases of mental confusion in the puerperium also responded well to the treatment.—H. Hoff and J. A. Shaby, *Lancet*, i/1940, 27.

**ENTERIC FEVER.** All but one of 15 cases of enteric fever (7 typhoid, 8 paratyphoid) showed immediate improvement following intravenous injection of suprarenal cortex extract and vitamin C. As soon as diagnosis is established intravenous injections of suprarenal cortex extract are begun, in doses between 5 and 20 ml., according to the age and state of the patient, the usual daily dose being 10 ml. with 500 to 1000 mg. of vitamin C. The two products are mixed in the same syringe. During the same day two more doses of 500 mg. vitamin C are injected at 4-hourly intervals. The combined administration is continued for 5 to 12 days and is followed by two intravenous injections daily of 500 ml. of vitamin C alone for at least 7 days. The effect is dramatic from the first injection, and there is no pain, shock, or reaction. There is abundant urination and a gradual fall of temperature to normal between the third and seventh day. Three cases of acute *B. coli* infection were also successfully treated in the same way.—Najib-Farah, *Lancet*, i/1938, 777.

**PAGET'S DISEASE** is favourably influenced by treatment with adrenal cortex. The high blood phosphatase tends to fall to normal, with improvement in clinical symptoms.—L. Berman, *Endocrinology*, 1936, 20, 226.

Used with benefit in 9 cases. Cortin was given intramuscularly in amounts of 5 to 10 ml. or more per week. In the majority of cases there was undoubted clinical improvement. Injections of desoxycorticosterone acetate and oral administration of adrenal cortical extract did not give such good effects.—E. M. Watson, *Canad. med. Ass. J.*, ii/1939, 561.

**VOMITING OF PREGNANCY.**—Nausea and vomiting of early pregnancy treated by desiccated suprarenal cortex, orally; also temporary improvement from cortex extract, intravenously.—W. N. Kemp, *Endocrinology*, 1932, 16, 434.

Improvement in 173 early cases of vomiting of pregnancy by subcutaneous injection of extract of suprarenal cortex for several days, followed by 9 to 12 gr. of desiccated suprarenal gland, reduced later to 6 gr. daily.—W. N. Kemp, *Med. Rec.*, N.Y., 1934, 14, 239.

[P1-S7] **Adasperlen** (*Endocrines-Spicer, Watford*). Each ml. contains total adrenal 16 gr., and extract of reticulo-endothelial structures in a glycerinated solution for oral administration in asthenic conditions. *Dose*.—2 to 10 drops thrice daily in water at meals.

[P1] **Cortin Organon** (*Organon Laboratories, London*). Liquid extract of suprarenal cortex. 1 ml. equivalent to 50 g. of whole gland.

[P1] **Eschatin** (*Parke, Davis, London*). 1 ml. represents 40 g. of suprarenal cortex. *Dose*.—Severe cases, 10 ml. intravenously every 3 or 4 days; in less severe cases, 1 to 5 ml. subcutaneously.

[P1] **Eucortone** (*Allen & Hanburys, London*). 1 ml. is equivalent to 75 g. of suprarenal cortex or approximately 110 g. of whole gland.

[P1] **Supracort** (*Paines & Byrne, London*). 1 ml. represents 75 g. of fresh suprarenal cortex.

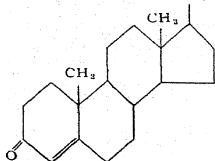
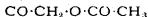
**Suprarenal Cortical Hormones.** Following the preparation of active extracts from the cortex of the suprarenal gland, further research culminated in the isolation in crystalline form of a number of active principles, the most potent of which was corticosterone with the empirical formula  $C_{21}H_{30}O_4$ . Shortly afterwards another substance, desoxycorticosterone, was artificially prepared from stigmasterol, a plant sterol occurring in the soya bean, and has proved to have ten times the activity of corticosterone. Since its artificial preparation desoxycorticosterone has been isolated from natural sources. As in the sex hormones, esterification of the cortical hormones prolongs and intensifies their action, and desoxycorticosterone is now obtainable in the form of its acetate for clinical use.

It has been shown that the adrenal cortex does not elaborate any single substance which can be described as the vital hormone of this gland. An extract of the adrenal cortex contains a surprisingly large number of closely related steroid derivatives which have specific effects qualitatively different one from the other. Substitution therapy in adrenalectomised animals is inadequate unless the hormones which influence gluconeogenesis and the efficiency of muscles are given together with the hormones that influence renal function and the distribution of water and the electrolytes.—E. C. Kendall, *Proc. Mayo Clin.*, 1940, 297.

**Corticosterone.**  $C_{21}H_{30}O_4 = 346.36$ . It has been isolated from the adrenal glands and from animal urine as a colourless, crystalline substance giving a strong fluorescence with sulphuric acid. Corticosterone differs from desoxycorticosterone in having a hydroxyl group on carbon atom 11. It melts at  $180^\circ$  to  $182^\circ$  and is soluble in alkalis and organic solvents.

Rat experiments indicate that pure corticosterone in aqueous solution is very effective in combating shock. Desoxycorticosterone is ineffective under similar conditions. The relative inefficiency of adrenal cortical extracts is probably due to the fact that the beneficial effects of the corticosterone are in part counterbalanced by harmful contaminating substances.—H. Selye and C. Dosne, *Lancet*, ii/1940, 70.

**Desoxycorticosterone Acetate.** *Prop. Names.* D.O.C.A. (*Organon Laboratories, London*), CORTIRON (*Schering, London*), PERCORTEN (*Ciba, Horsham*), SYNCORTYL (*Roussel Laboratories, London*).



= 372.5

**Dose.**—2 to 15 mg. by intramuscular injection.



Desoxycorticosterone acetate occurs in the form of fine needles melting at 157° to 159°, and soluble in oil.

**Uses.** The most important use of desoxycorticosterone acetate is in the treatment of Addison's disease in which its therapeutic action is similar to that of cortical extract, though there is evidence that it does not yield complete adrenal cortical replacement. It is usually given by intramuscular injection in oily solution in a dose of 5 to 10 mg. daily at the beginning of treatment, and 5 to 15 mg. weekly as a maintenance dose. There is usually a striking and continued improvement in the condition of the patient and the blood chemistry findings are restored approximately to normal. As an alternative method of administration, tablets containing 50 to 150 mg. may be inserted under the skin; good results are claimed for this method, but it is not recommended for patients in crisis.

The use of the substance is not devoid of risk; hypoglycæmia, oedema and hypertension are not uncommon complications and some deaths have been reported. It should only be employed where there are adequate facilities for recognising and dealing with any difficult situations which may arise during the course of treatment.

Originally this treatment was combined with a restriction of the potassium intake and an increase of the sodium intake, a measure essential to the success of treatment with cortical extract. Recent work, however, indicates that patients suffering from Addison's disease are able to tolerate a liberal intake of potassium when treated with desoxycorticosterone acetate, that excessive retention of salt and water occurs very readily when the intake of potassium is restricted, and conversely that a liberal intake of potassium has a tendency to counteract such retention. It would appear, therefore, that the use of the low potassium diet and the administration of extra sodium are not necessary in the treatment of Addison's disease with desoxycorticosterone acetate, and it is probable that the incidence of complications following the use of this substance will be reduced as the result of this modification in procedure.

In addition to its use in Addison's disease it is also of value in minor conditions of adrenal insufficiency. There are good grounds for believing that such a deficiency occurs for instance in the case of severe burns, in surgical and traumatic shock, and in acute infectious diseases such as diphtheria, and intramuscular injections of 5 to 10 mg. daily have been employed with considerable benefit in such conditions.

**ADDISON'S DISEASE.** Desoxycorticosterone acetate was found effective in two patients with Addison's disease. It has a therapeutic action in Addison's disease similar to that of cortin. From the cases recorded it appears that 6 mg. of desoxycorticosterone acetate (1 ml. of oily solution) is equivalent to more than 5 ml., but less than 20 ml. of cortin.—S. L. Simpson, *Lancet*, ii/1938, 557.

The implantation of tablets of desoxycorticosterone acetate into the anterior abdominal wall brought about a prolonged improvement in the condition

of a patient suffering from Addison's disease and also a return of his urinary sodium concentration towards normal values.—H. W. Dryerre, *Brit. med. J.*, i/1939, 971.

In six patients who could not be maintained in a good condition by the administration of sodium chloride therapy alone, pellets of crystalline desoxycorticosterone acetate, weighing 50 to 150 mg. each, were inserted under the skin in the infracapular region. There was a striking and continued improvement in all the patients. It was noted that one pellet of 100 to 150 mg. was required as a substitute for each 0.5 mg. of hormone in oil, and pellets weighing 50 to 150 mg. were absorbed at a rate of 0.25 to 0.35 mg. per day. No untoward reactions or signs of local discomfort were noted. This form of treatment is recommended as a substitution therapy for patients who have been restored to some degree of health by daily injections of hormone, but it is not recommended as suitable for patients in crisis. Additional sodium chloride therapy reduces the amount of desoxycorticosterone acetate required.—G. W. Thorn *et al.*, per *Practitioner*, ii/1939, 349.

The use of desoxycorticosterone esters (acetate or propionate) in patients with Addison's disease produces striking clinical and physiological effects, but extreme caution must be exercised, since excessive dosage may lead to the development of hypoproteinemia, marked oedema and cardiac insufficiency.—J. W. Ferrebee, *J. Amer. med. Ass.*, ii/1939, 1725.

The effect compared with that of aqueous cortical extracts in the treatment of Addison's disease. Patients have an increased sense of well-being on desoxycorticosterone acetate, and blood pressure and blood chemistry findings are restored approximately to normal. It has the advantage that it can be given in small injections and is less painful than cortin, but owing to the slow rate of absorption from the oily solution in which it is contained, it is of little use at times of severe crisis with serious vascular collapse.—R. A. Cleghorn *et al.*, *Canad. med. Ass. J.*, ii/1939, 226.

Striking and continued improvement in 21 out of 30 cases. The quantity of supplementary sodium chloride must be regulated carefully during treatment, since excessive doses of desoxycorticosterone acetate and added sodium chloride may result in the appearance of oedema, hypertension, and congestive heart failure.—G. W. Thorn and W. M. Firor, *J. Amer. med. Ass.*, i/1940, 2517.

Though clinical benefit followed its use in every one of 6 cases, there is evidence that it does not yield complete adrenal cortical replacement, and for the present it is not in the best interest of the patient to depend on desoxycorticosterone to the exclusion of adrenal cortex extract in the presence of crisis or if some symptoms are uncontrolled.—E. P. McCullagh and E. J. Ryan, *J. Amer. med. Ass.*, i/1940, 2530.

Given as the only form of replacement therapy in Addison's disease it does not appear to provide complete substitution for the normal adrenal cortex. It is highly probable that desoxycorticosterone does not represent the true hormone of the adrenal cortex, but only one of the physiologically active sterols produced by that gland, some additional factor or factors being necessary to restore the metabolic processes to normal in adrenalectomised animals. The known complications which may arise from the clinical use of desoxycorticosterone make its therapeutic use a procedure involving some risk, and until many details of its action are more thoroughly understood its use should probably be restricted. The complications of oedema and hypertension may be adequately controlled by reducing the intake of sodium salts to normal or even subnormal levels. Not only has it been found possible to allow normal quantities of potassium in the diet, but it has been found beneficial in some cases to administer extra potassium.—E. S. Gordon (Report of the Council on Pharmacy and Chemistry of the A.M.A.), *J. Amer. med. Ass.*, i/1940, 2549.

The tolerance of patients suffering from Addison's disease to potassium while such patients are being treated with desoxycorticosterone acetate.—T. B. Tooke *et al.*, *Proc. Mayo Clin.*, 1940, 353.

All cases in a state of crisis must receive cortical extract, or cortical extract plus desoxycorticosterone, salt and glucose. Mild chronic cases may keep in good health by taking up to 20 g. of extra salt daily. Moderate cases can be treated satisfactorily with salt and with desoxycorticosterone given either by injection or by implanted pellets. Several cases require salt, implanted pellets of desoxycorticosterone, and also small supplementary doses of cortical extract.—*Lancet*, ii/1940, 201.

**BURNS.** Successfully used in 8 cases of established toxæmia in children. A very definite clinical improvement took place coincidentally with the administration of the drug given in an average dose of 6 mg. intramuscularly every 2 hours; or it may be given intravenously by adding to the reservoir of the continuous drip (dextrose-saline) apparatus.—W. M. Dennison, *Lancet*, ii/1939, 1108.

**MYASTHENIA GRAVIS** treated by hypodermic injections of desoxycorticosterone acetate and by implantation of three pellets (150 mg. each) into the subcutaneous tissue of the abdomen; improvement both striking and dramatic.—R. C. Mochlig, *J. Amer. med. Ass.*, ii/1940, 123.

**SHOCK.** Desoxycorticosterone, which is most active in maintaining adrenalectomised animals, proved to have little if any effect in combating shock, even if large amounts were administered in divided doses. From this it may be concluded that some substance other than desoxycorticosterone is responsible for the high activity of the cortical extracts. In view of the fact that carbohydrate metabolism is seriously disturbed in shock, and that corticosterone is much more active in influencing carbohydrate metabolism in cases of adrenal insufficiency than desoxycorticosterone, it appears that the former might be responsible for the shock-combating effect of our cortical extract, which contains both these compounds. Until corticosterone becomes commercially available, active cortical extracts must be regarded as the most powerful hormonal agents which can be used for combating shock.—H. Selye *et al.*, *Canad. med. Ass. J.*, ii/1940, 7.

Adrenal cortical extract and desoxycorticosterone acetate given together both before and after trauma without other therapy, reduce the mortality from experimental shock in normal (non-adrenalectomised) rabbits. The difference in mortality between the treated and control animals is highly significant. Desoxycorticosterone acetate alone, given before trauma, is not effective, for the difference in mortality between this group and the controls is not statistically significant.—P. G. Weil *et al.*, *Canad. med. Ass. J.*, ii/1940, 11.

[P1] **Cortenil** (*Bayer Products, London*). Synthetic cortical suprarenal hormone preparation; 1 ml. = 5 mg. desoxycorticosterone acetate. *Dose.*—1 ml. once or twice daily intramuscularly. Addison's disease, asthenia, debility, severe burns and other conditions where there may be hypofunctioning of the cortical tissue.

[P1] **Cortigen** (*Richter, London*). 1 ml. contains 4 cortico-dynamic units of the suprarenal cortical hormone. *Dose.*—1 ml. daily, subcutaneously or intramuscularly.

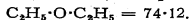
**Kidney.**—Kidney substance has been given in nephritis and other kidney troubles, but the evidence of its value is conflicting.

Massive treatment said to be essential. Phenolphthalein should not be given simultaneously.

**Nephritin Tablets** (*Reed & Carnrick, Jersey City; Coates & Cooper, London*). Contains the hormones and internal secretions of the kidneys. *Dose.*—Four tablets four to eight times a day. *Dose* to be reduced as improvement occurs. For treatment of acute and chronic nephritis.

## ÆTHER.

*B.P., P. Dan., P. Jap. V.*



*Syn. ÆTHER DEPURATUS (Fr. Cx.), ÆTHER SULPHURICUS, ETHYL OXIDE (U.S.P. XI), SOLVENT ETHER.*

*Dose.*—15 to 60 minims (1 to 4 ml.).

Æther is diethyl ether and is prepared by distilling a mixture of ethyl alcohol and sulphuric acid, with rectification of the distillate. The use of sulphuric acid gave rise to the misleading term "sulphuric ether," a name which rightly belongs to ethyl sulphate.

Ether is a colourless, transparent, very mobile liquid, with a characteristic odour and a sweet, burning taste. It volatilises very quickly and by so doing produces great cold. Although ether is one of the lightest of liquids its vapour is very heavy, being  $2\frac{1}{2}$  times heavier than air. Only the quality of ether designated in the *B.P.* Anaesthetic Ether should be used as an anæsthetic. The quality described as Ether is suitable for general purposes and for use in chemical analysis. To emphasise this difference the Committee on General Chemistry of the Pharmacopœia Commission (*Report* 14) have recommended that the quality described as Ether should be named Æther Solvens, Solvent Ether.

Methylated ether for various technical purposes is prepared from industrial methylated spirit, or from duty-free alcohol with subsequent denaturation by the addition of wood naphtha. It can be obtained with specific gravities varying from 0.720 to 0.750. Methylated ether is unsuitable for both anæsthetic purposes and oral administration.

**Caution.** Ether is very volatile and inflammable and care must be taken not to use it near a flame. Mixtures of its vapour with oxygen, nitrous oxide or air in certain proportions are explosive.

**Soluble** 1 in  $8\frac{1}{2}$  of water, and the ether similarly dissolves about the same amount of water. Is miscible in all proportions with alcohol. Ether is a solvent for a number of alkaloids, fats, resins, and of mercury perchloride and biniodide, also of bromine and iodine.

**Antidotes.** Treat as for poisoning by chloroform, see p. 401.

**Uses.** Internally ether is a rapid stimulant in syncope. Is carminative and may relieve dyspepsia and asthma. Hypodermically it may save many cases of syncope, collapse, and shock from hæmorrhage and injury, and intramuscular injections of 1 to 2 ml. have been employed in the treatment of whooping cough.

Ether has been used as an antiseptic dressing for wounds, and it is used as a menstruum and vehicle for skin medication, on account of its solvent action on sebaceous secretion. This solvent action has also been employed for dissolving gall-stones, the ether being injected into the common bile duct.

**BRONCHITIS (post-operative).** Intramuscular injection of 0.5 ml. of ether in 0.5 ml. olive oil, with the addition of a local anæsthetic. One such injection daily recommended in every case of acute or chronic bronchitis without emphysema.

**GALL-STONES.** Fragmentation of a stone in the common bile duct, and expulsion of the fragments into the duodenum, was accomplished by 3 daily injections each of 5 ml. of ether and 2 subsequent injections of a mixture of  $\frac{1}{2}$  ethyl alcohol and  $\frac{1}{2}$  ether.—W. Walters and H. R. Wesson, *Proc. Mayo Clin.*, 1937, 260.

The removal of gall-stones remaining in the common bile-duct after operation may be successfully achieved by the injection of ether into the duct. Following operation, a drain is inserted into the common duct and a few drops of ether are injected into the drain several times daily. This causes the stones to dissolve and the passage of the softened stones is facilitated by the injection of a small quantity of liquid paraffin. The method was successful in every one of 38 cases.—R. O. Pribram, *Lancet*, 1/1939, 1311.

The injection of ether into the biliary tract to dissolve gall-stones at first consideration appears to be a heroic measure, but it has been done in enough instances to make one feel safe in its use when done properly, though it can be applied only in a limited number of cases. The stone must be soluble, *i.e.*, either pure cholesterol or formed of small fragments bound together by cholesterol, and it must be so situated that it may be bathed directly with the solvent used.—C. M. Burgess, *J. Amer. med. Ass.*, i/1940, 2372.

OTITIS MEDIA, suppurative, has been treated by ether which is run into the affected ear and allowed to evaporate.

SCIATICA has been treated by injection of ether with either cocaine or morphine subcutaneously into the sciatic nerve. 5 minim doses of ether with 2 minims of 1 in 12 cocaine, or morphine injection 3 minims, using a 2½-inch needle.

WHOOPIING COUGH has been treated by ether injected intramuscularly in the buttock. Supposed to act by combating the spasmodic element of the disease. 1 ml. up to age of 7 or 8 months, and in older children 2 ml. repeated daily or on alternate days; also useful in broncho-pneumonia.

Provided there are no complications such as bronchitis or broncho-pneumonia present, whooping cough may be subdued within three weeks by the oral administration of ether. The following prescription is effective, inexpensive and pleasant to take: ether 2 m., tincture of quillaia 1 m., syrup simplex 30 m., water to 60 m. This represents a simple dose to be taken every 2 hours. For a day or two there may not be any marked change, but after that improvement is rapid and continuous, the paroxysms becoming less in frequency and severity until they cease altogether. Parents should be warned to keep the mixture in a cool place, tightly corked, and to avoid proximity to a naked flame when pouring out a dose.—W. T. Milton, *Brit. med. J.*, i/1938, 919.

### Mistura Ætheris cum Ammonia (B.P.C.).

*Dose.*—½ to 1 ounce (15 to 30 ml.).

Contains 30 m. each of spirit of ether and aromatic spirit of ammonia in camphor water to 1 fl. oz.

*St. T. H.* has same ingredients with chloroform water, with *syn.* "PATENT"; with 1 gr. of camphor per oz., "CAMPHORATED PATENT." A rapid stimulant. *Gt. Örm. H.* has (for child 1 year old) spirit of ether 3½ m., aromatic spirit of ammonia 3½ m., tincture of orange 2 m., chloroform water to 1 dr.

*Mist. Æther. (N.I.F.).* Ether 10 m., ammonium carbonate 4 gr., syrup of orange 15 m., water to ½ oz.

**Spiritus Ætheris (B.P.).** Ether 33% *v/v*, in alcohol (90%).

*P. Belg. IV* has ether 468, alcohol (94%) 532; *P. Ital. V* ether 1, alcohol (95%) 1; *F.E. VIII* ether 4, alcohol (90%) 1; *P. Dan.*, *P. Jap. V* and *P. Helv. V*, ether 1, alcohol 3; *Fr. Cx.*, ether 1, alcohol (90%) 1.

*Dose.*—15 to 60 minims (1 to 4 ml.).

The older formula is occasionally prescribed; *viz.*:—

**Spiritus Ætheris Compositus (B.P.C.).** *Syn.* HOFFMANN'S ANODYNE, LIQUOR HOFFMANNI, but the simple spirit of ether is now called Hoffmann's anodyne abroad.

*Dose.*—1 to 1½ drachms (4 to 6 ml.) for a single administration; 20 to 40 minims (1·2 to 2·5 ml.) for repeated administration.

An alcoholic solution of ether, about 1 in 8, with ethyl sulphate and ethyl hydrogen sulphate.

**Syrupus Ætheris (Fr. Cx.).** Ether 2%, alcohol (95%) 5%, water 23%, cold-prepared simple syrup 70%.

**Æther Anæstheticus (B.P.).** *Syn.* ÆTHER ÆTHYLICUS (*Fr. Cx.*), ÆTHER PURIFICATUS, ÆTHER (*U.S.P. XI, P. Ned. V, P. Helv. V, P. Belg. IV, P. Ital. V and F.E. VIII*), ÆTHER PURISSIMUS, ETHER OFFICINALIS, ÆTHER PRO NARCOSI (*P. Jap. V, P. Dan.*).

Limit tests are included for peroxides, acetone and aldehyde, and methyl compounds, which may cause unpleasant post-operative effects.

Anæsthetic ether should be stored in well-stoppered, amber bottles wrapped in black paper.

Storage of anæsthetic ether over solid caustic potash in dark bottles is recommended. Peroxidation is retarded and aldehyde formation accelerated by iron; decomposition of ether is increased in presence of light. It may also be preserved for 8 to 9 months without a stabiliser in the presence of iron, provided the products of reduction of the initial peroxides are removed.—A. Monkov, Z. Larionov and N. S. Gorgainova, per *Brit. chem. Abstr. (B)*, 1939, 212.

**Mixtura Anæsthetica Composita (Fr. Cx.).** *Syn.* SCHLEICH'S ANÆSTHETIC MIXTURE. Ether 30, chloroform 10, ethyl chloride 5, all by weight.

### **Anæsthesia with Ether.**

Ether is almost universally considered safer than chloroform, and the occasional sudden deaths in the early stages of induction with chloroform, from cardiovascular inhibition due to vagal stimulation or from ventricular fibrillation, are unknown with ether, as also is the delayed poisoning which may follow the administration of chloroform. On the other hand, ether is more irritant to the mucous membrane and induces hypersecretion of mucus in the air passages; consequently there is an increased liability to inhalation pneumonia. The secretion of mucus by the stomach and the activity of the salivary glands are also stimulated, thus increasing the tendency to post-operative nausea and vomiting. This excessive secretion is greatly diminished by the pre-operative injection of 1 to 2 gr. of atropine sulphate, but ether must not be used where there is any affection of the trachea, bronchi or lungs. It has a toxic action on the liver and kidneys, and prolonged administration is contraindicated if there is any lesion of these organs. Ether has less effect than chloroform on blood pressure, and capillary oozing is therefore less easily controlled. Induction by ether alone is very unpleasant, and some other anæsthetic such as nitrous oxide or admixtures of ether with chloroform in various proportions are commonly employed until the second stage is reached.

For the production of anæsthesia ether may be administered by inhalation, in which the anæsthetic is vaporised by the patient's breathing, by insufflation, in which the previously vaporised anæsthetic is introduced directly into the mouth, pharynx or trachea by means of a suitable apparatus (*e.g.*, Shipway's), or rectally in oily solution. Other methods of administering ether have been proposed, such as delivery of ether vapour directly into the rectum, intravenous injection of a solution of ether in normal saline, or oral administration of 1 to 2 oz. of a mixture of equal parts of ether and liquid paraffin.

Administration as an inhalation anæsthetic may be by the "open," "semi-open" or "closed" method. In the former a piece of gauze tissue with a hole for the mouth and nose is placed loosely on the face, and above it is placed a wire mask (e.g., the Schimmelbusch) covered with a layer of gauze and a further layer of gauze tissue with a hole through which the anæsthetic is dropped on to the gauze. Air can enter around the edges of the mask as well as through it, in distinction from the semi-open method in which the mask fits the face more closely and is covered so as to prevent access of air. In this method expired air is re-breathed, and there is less chilling from evaporation of the ether; an adequate concentration of anæsthetic is thus more easily obtained and induction occurs more rapidly. Air must be admitted periodically in order to prevent asphyxiation. In the closed method the patient breathes into and from a bag into which air and the vapour of the anæsthetic are admitted as required by the anæsthetist.

The smell of pure ether, if used for induction, may be masked by the addition of oil of orange. Gwathmey has recommended the use of 1 oz. of "essence of orange" (oil of bitter orange 1, dehydrated alcohol 3) and 3 oz. of ether, in the hot-water bottle of the Gwathmey three-bottle apparatus.

When ether is to be employed for operations in which the presence of the mask would interfere, after induction by inhalation the anæsthetic may be administered by insufflation by means of a tube passed through the nose or mouth, according to the site of the operation, so that the vapour is delivered directly into the pharynx (intraparyngeal) or trachea (endotracheal). For endotracheal administration the insertion of the tube between the vocal cords is controlled with the aid of a laryngoscope, unless the condition of the mouth precludes its use. Intubation procedures may also be used with inhalation anæsthesia, but in this case the pharynx must be packed with lubricated plugs or in other ways, so as to prevent air being drawn in otherwise than through the tube.

Endotracheal anæsthesia is the method of choice for all operations on head, nose, mouth, and throat where satisfactory anæsthesia cannot be maintained with a free airway by the ordinary methods without inconvenience to the surgeon. When there is blood in the upper air passages it is a necessity.

Occasionally convulsions occur in patients under deep ether anæsthesia. It was at one time thought that these were due to the presence of impurities, such as peroxides or aldehydes in the ether, but proof of this was lacking. On the other hand, there is considerable evidence to show that the high temperature of the operating theatre, especially during the summer months, and the previous administration of atropine, are contributory causes. (*For a more detailed discussion of this subject see previous edition*).

**CONVULSIONS.** Description of 2 cases, 1 fatal. In both cases the ether in the bottle on the Boyle's machine was used for other patients with no ill-effects, and the same machine had been used, and the details of administration of the anæsthetics were the same as in 257 other patients anæsthetised during the previous 2 months.—H. G. Earnshaw, *Brit. med. J.*, ii/1937, 880.

*The treatment for other convulsions is the early administration of even a small dose of Evipan.*—H. Bailey, *Brit. med. J.*, ii/1940, 222.

#### **Gwathmey's Oil-Ether Rectal Anæsthesia.**

This method of anæsthesia may usefully be employed for laryngoscopic and bronchoscopic examinations and for operations on the mouth, nose, and throat. For rectal administration of ether the bowels are emptied by a cathartic given the previous evening and an enema on the morning of the operation. The anæsthetic is administered as a solution in olive oil, anæsthesia being complete in about 20 minutes and lasting for  $\frac{1}{2}$  to 1 hour. The following dosage has been recommended: For children under 6 years a 50% solution is used, allowing 1 oz. for every 20 lb. of body weight. This is non-irritating and no preliminary medication is wanted. Between 6 and 12 years use 55 to 65% solution without preliminary medication. Keep the patient quiet and allow 20 to 30 minutes for the full effect. Use 1 oz. for every 20 lb. body weight as before. Between 12 and 15 years use the same percentage and amounts, with possibly the addition of  $\frac{1}{2}$  gr. of morphine and  $\frac{1}{600}$  gr. atropine hypodermically as a preliminary. From 15 years upwards a 75% mixture is used with the same amount as before, 1 oz. to every 20 lb. It will be seen, therefore, that for an *adult* weighing about 160 lb., 8 oz. of the mixture would be wanted (i.e., ether 6 oz. and olive oil 2 oz.).

The 8 oz. should be passed in slowly, *i.e.*, it should take 5 minutes. A maximum strength of 65% is now advised by Gwathmey. The bowel should be washed out immediately after the operation and Vaseline smeared on the buttocks and thighs to avoid irritation from escaping ether.

Rectal ether and olive oil has many advantages over inhalation, *e.g.*, ease of administration, absence of apprehension in patient, and of coughing, retching, and straining, reduction of shock, and absence of post-operative vomiting.

Chief among the disadvantages is that depth of anaesthesia is not under such control as with inhalation. It causes irritation of the intestines. Must not be used in room with open flame.

In a series of 5000 anaesthetics slight diarrhoea occurred in only 6 cases and no deaths. (The retention enema now appears to consist of a 2 to 1 ether oil mixture with the addition of 2 dr. of paraldehyde.) A full description of technique is given. Has wider limits of safety than any inhalation method. Any pathologic condition of the bowel a contraindication.—J. T. Gwathmey, *J. Amer. med. Ass.*, *ii*/1929, 447.

Safe and easily controlled, to use in all bad surgical risks. Leaves minimum of bad effects after operations lasting many hours.—W. Wood, *Brit. med. J.*, *ii*/1929, 1156.

### ***Synergistic Method of Painless Childbirth (Rectal Ether Analgesia).***

This method depends on the supposed synergistic action of magnesium sulphate and ether, much smaller doses of both being necessary than when either is used alone. As originally advocated by Gwathmey, the procedure was as follows: when the os will admit three fingers, 0.006 g. ( $\frac{1}{16}$  gr.) of morphine in 2 ml. of a 50% solution of magnesium sulphate is injected intramuscularly. The injection is repeated in 2 or 3 hours if the pain is not relieved. At the same time, an enema composed of ether 70 parts, alcohol 8, quinine hydrobromide 0.6, and olive oil to 120 parts, is administered. Sometimes a mixture of ether 90 and chloroform 10 is used instead of ether alone.

The method is not claimed to give painless childbirth, but it gives great relief during the agonising part of the ordeal in some 90% of cases, without bad effects on mother or child.

The disadvantages are the intricacy of technique, the length of time that must be spent at the bedside, the necessity of isolating the patient, and the possibility of proctitis following the introduction of ether into the rectum.

Gwathmey's original technique has now been modified in certain respects, as follows:

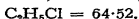
The formula for the rectal mixture as now used is ether  $2\frac{1}{2}$  oz., quinine alkaloid 20 gr., alcohol 45 m., paraldehyde 2 dr., and liquid petrolatum or olive oil to 4 oz. The technique has been modified by the omission of the magnesium sulphate injection and the substitution of Nembutal by mouth; by the use of the degree of the patient's suffering instead of the amount of cervical dilatation as a time criterion for administration of sedatives and rectal instillations; by the substitution of a 5 to 10% solution of sodium bicarbonate (a heaped teaspoonful in a quart of water) for the soapsuds enema. If the Nembutal is not given within 8 hours after the initial enema the enema is repeated. The enema should not be given just before the rectal instillation—if this is unavoidable, any remaining water is siphoned back before the rectal instillation. Instead of the first two injections of magnesium sulphate the patient is given orally 3 gr. and  $1\frac{1}{2}$  gr. respectively of Nembutal;  $\frac{1}{2}$  or  $\frac{1}{4}$  gr. of morphine is usually given hypodermically with the second dose of Nembutal in a primipara in active labour, but if the labour is not uncomfortably active or is of the prolonged type, the second dose of Nembutal may be repeated once or oftener before the morphine is given (not more than 10 to 12 gr. in 24 hours). When the effects of the



morphine begin to wear off the ether-oil-quinine solution is given per rectum and repeated as often as required, omitting the quinine after the second instillation. Omit morphine if delivery is anticipated within 4 hours—if it is anticipated within 4 hours the Nembutal and the rectal instillation are promptly given simultaneously. During the administration of the instillation the patient is told to breathe deeply, with mouth open, and to draw up with the anal sphincter. After all the ether mixture is passed out of the catheter, the catheter is clamped to prevent air being drawn into the rectum. The catheter is then gently withdrawn and pressure made with a towel over the anus during 3 or 4 contractions. The instillation may be given at intervals of 2½ hours if necessary. At delivery, ethylene, nitrous oxide or ether is given by inhalation, but *not* chloroform. When the baby is born, if a gas-oxygen apparatus is used, all anæsthetic is cut off and 5% carbon dioxide and oxygen under pressure is given before the cord is cut. It is the safest of all satisfactory analgesias used to date. Several series of many thousands of cases have been reported, no maternal or infant mortality being attributed to its use. In addition, the patient rarely has more than a vague recollection of the labour. There are no major physical contraindications, it is not likely to prolong labour, and the baby suffers no ill-effects.—J. T. Gwathmey and C. O. McCormick, *J. Amer. med. Ass.*, ii/1935, 2044.

## ÆTHYLIS CHLORIDUM

B.P., P.G. VI, U.S.P. XI, Fr. Cx.



*Syn.* CHLORYL ANÆSTHETIC, ÆTHANOLI CHLORIDUM (P. Belg. IV).

At ordinary temperatures ethyl chloride is gaseous, but condenses when slightly compressed into a colourless mobile liquid with a sweetish burning taste. Slightly *soluble* in water, readily in alcohol. Sp. gr. about 0.921 at 0°.

**Antidotes.** Treat as for poisoning by chloroform, see p. 401.

**Uses.** Its main use is as a local anæsthetic by freezing and as a general anæsthetic by inhalation. On account of its low boiling-point (about 12.5°) and the intense cold produced by evaporation, it is effective as a local anæsthetic in minor surgery, also for neuralgia. The part should be washed with soap and then with alcohol or ether before applying. In dental cases the patient is instructed to breathe through the nose during operation, the part is well dried, and other parts protected. Its vapour is inflammable.

As a general anæsthetic ethyl chloride is not unpleasant; induction is rapid, occupying a minute or less, and recovery is also rapid although some patients experience nausea and malaise for a short time. As a single anæsthetic its main use is for minor surgery, such as tonsillectomy and dental extractions, in children, by whom nitrous oxide anæsthesia is badly tolerated owing to oxygen deprivation. In both adults and children it is useful for induction prior to maintenance with ether, the latter being administered as soon as breathing becomes regular. When used alone it produces an anæsthesia lasting for 1 to 2 minutes followed by analgesia for a further 30 to 40 seconds. It may be administered by either the semi-open or closed method (*vide* Ether), the latter being adopted for children (*e.g.*, using the Loosely bag).

Cardiac failure may occur as with chloroform, and there may be muscular spasm making artificial respiration difficult owing to rigidity of the chest wall.

Nasal administration of ethyl chloride.—R. B. Gould, *Brit. med. J.*, i/1934, 1073.

DENTAL EXTRACTIONS under ethyl chloride at Gt. Ormond St. Hospital for Sick Children found satisfactory. Closed method with a Loosely bag is used. 60 to 180 seconds' surgical anaesthesia.—H. Sington, *Brit. med. J.*, i/1930, 217.

**Thilocologne** (Coates & Cooper, London). A brand of ethyl chloride and eau de Cologne.

**Anestile** (Bengué, London). A mixture of ethyl chloride and methyl chloride for use as a local anaesthetic.

**Ethylis Bromidum** (B.P.C., P.G. VI, Fr. Cx., P. Jap. V, P. Helv. V, P. Belg. IV, F.E. VIII, P. Ital. V). *Syn.* HYDROBROMIC ETHER.  $C_2H_5Br = 109.0$ .

A colourless, very volatile liquid with a strong peculiar odour and a sweetish warm taste. Contains 1% of alcohol to prevent it becoming brown on exposure owing to decomposition and liberation of bromine. Sp. gr. 1.453 to 1.457. B.p. about 38°.

**Soluble** 1 in about 100 of water, and miscible with alcohol 90% and ether.

Has been used by inhalation for short general anaesthesia but is too potent a respiratory depressant.

For local anaesthesia it may be used as spray. For neuralgia it may be applied directly to the skin and covered for a short time. Capsules encased in cotton wool and silk, and containing 5 minims in each, are convenient for use by inhalation when crushed. They are useful in asthma and epileptic convulsions.

**Ethyleni Dibromidum**.  $C_2H_4Br_2 = 187.9$ . *Dose*.—1 to 2 minims in alcoholic solution or oily solution hypodermically, or in gelatin capsules. A colourless liquid of sp. gr. about 2.18.

**Ethylis Iodidum**. *Syn.* HYDRIODIC ETHER.  $C_2H_5I = 156.0$ .

*Dose*.—By inhalation, 3 to 5 minims (0.2 to 0.3 ml.).

May be obtained by distilling a mixture of alcohol, iodine and phosphorus. A colourless, non-inflammable, heavy liquid with a penetrating odour. It is liable to become coloured on exposure to air and light owing to liberation of iodine. B.p. 71° to 72°; sp. gr. about 1.943.

**Soluble** 1 in 440 of water; miscible with alcohol and ether.

**Uses**. It is useful *inhaled* either alone or mixed with twice its volume of chloroform to relieve the dyspnoea of bronchitis, whooping cough and bronchial asthma. As it contains four-fifths of its weight of iodine, it forms a rapid means of saturating the system with this element; iodine can be detected in the urine 10 minutes after inhalation, and as long as 30 hours after; it neither impairs appetite nor weakens digestion.

In bronchial catarrh it induces sleep and promotes expectoration when inhaled. It is useful for inhalation in oedema of the glottis from catarrhal laryngitis. It acts as an antispasmodic in angina pectoris, spasmodic asthma and certain forms of nervous dyspnoea.

Inhalations have also been successfully employed in the treatment of fungous diseases of the skin.

For inhalation it may be obtained in capsules enclosed in cotton wool and silk and containing 5 minims. The capsules are broken by pressure when required. Capsules are also obtainable containing 5 m. of ethyl iodide and 10 m. of chloroform.

*Externally* 10 to 20% ointment with paraffin basis may be used (stronger may blister). The system may be saturated with iodine by painting the iodide on the calf of the leg or between the shoulders, and covering with impermeable dressing.

**MYCOTIC AFFECTIONS OF THE SKIN** treated by ethyl iodide inhalations. A large amount of iodine enters the blood stream and only a small amount is returned in the venous blood, hence the tissues are exposed to large amounts. Inhale 1 ml. in about 20 minutes. Fungus cured. Should be tried in asthma, hypertension, and tertiary syphilis.—*Brit. med. J. Epit.*, i/1930, 62.

Ethyl iodide inhalations are a valuable means of combating the more severe and persistent fungous infections of the skin and mucous membrane. It should be tried for systemic fungous infections and should be of particular value in broncho-moniliasis. Begin with 2 ml. and increase by 0.5 ml. per dose until 4 ml. is reached, and continue with this dose. In systemic fungous infection doses as high as 5 and 6 ml. have been given without toxic effect. For children, these doses are halved. In order to avoid accumulation, treatment is omitted every third day, 48 hours being allowed to permit almost complete elimination of the accumulated iodide. It is important that the room be well ventilated during the inhalation, and the patient is advised to inhale and exhale through the mouth, the average time taken to inhale 2 ml. being about 20 minutes. The treatment is contraindicated in impaired excretory function of the kidney, in thyrotoxicosis and in active pulmonary tuberculosis. The complications following treatment are mainly cutaneous eruptions which clear up on discontinuance; peripheral neuritis occurred in 3 out of 244 cases, but cleared up in about 3 weeks. In 400 patients treated the average number of treatments required to obtain cure or improvement was as follows: epidermophytosis 27, psoriasis 40, tinea capitis 35, favus 50, blastomycosis 40.—J. H. Swartz, *Arch. Derm. Syph. N.Y.*, 1939, 40, 962.

**Methyl Iodide.**  $\text{CH}_3\text{I} = 142.0$ .

A colourless liquid (when first made) boiling at  $44^\circ$ . Sp. gr. 2.285. As a vesicant is even more powerful than cantharides.

Blisters may be produced in a few hours by rubbing in 15 to 20 drops.

**Methylis Chloridum.**  $\text{CH}_3\text{Cl} = 50.5$ . This gas, made by distillation of methyl alcohol, sodium chloride and sulphuric acid, is supplied compressed to a colourless liquid boiling at  $-21^\circ$ .

*Soluble* in water or alcohol, and readily soluble in ether and chloroform.

A local anæsthetic, valuable in neuralgia, sciatica and rheumatism. Spray the part for 5 or 6 seconds only. If effect too strong, apply glycerin. Effect may be reduced by covering the part with a thin layer of cotton wool.

**Antidotes.** Keep patient lying down and warm. Give fluids freely by mouth and enemas of 3% sodium bicarbonate with 5% dextrose. Avoid oils and fats. Oxygen inhalations if necessary. Potassium bromide, 60 gr. doses, may be required for the convulsions.

**METHYL CHLORIDE POISONING.** Possibility of toxic effects in this country due to its increasing use in refrigerators. The symptoms of poisoning are progressive drowsiness and apathy with nausea, vomiting and abdominal pain. Possibly muscular tremors and toxic convulsions with marked cyanosis. Pupils usually dilated; ptosis and nystagmus have been noted, also amblyopia. Temperature

risks, pulse and respiration rates are increased, blood pressure is lowered and the blood picture resembles primary anæmia. Anuria is usual in more severe cases and albuminuria occurs in about 50%; the urine is acid. Cerebrospinal fluid usually fairly normal but sometimes under pressure. *Treatment*.—Fresh air, oxygen, alkalis; choral or chloroform must not be used to control convulsions. Coramine as a cardio-respiratory stimulant. Rest in bed till temperature and pulse normal and nervous symptoms abated.—A. P. Gorham, *Brit. med. J.*, i/1934, 529.

Intoxication occurring among workmen at refrigerating works employing commercial methyl chloride. A toxic agent, cumulative in action and detected in urine as ammonium formate.—H. M. Baker, *J. Amer. med. Ass.*, i/1927, 1138. See also T. M. Legge and H. B. Porteous, *Brit. med. J.*, i/1930, 414, 751.

**Methylene Chloride.**  $\text{CH}_2\text{Cl}_2$  = 84.9. Has been used as an anæsthetic in Germany. Unsuitable for complete narcosis, but may be used to relieve the pains of labour by a process of intermittent administration.

## AGAR

*U.S.P. XI, P.G. VI, P. Svec. X, P. Helv. V, P. Dan., P. Jap. V, F.E. VIII.*

*Syn.* AGAR-AGAR, GÉLOSE (*Fr. Cx.*), JAPANESE ISINGLASS.

*Dose*.—1 to 4 drachms (4 to 16 g.).

Consists of a dried decoction of various species of *Gelidium* (Rhodophycæ). The sea-weeds are collected from rocks off the coast of Japan, bleached by exposure to the sun, boiled with water, and the filtered decoction concentrated by freezing or in other ways. The slabs so obtained are cut up and dried. It occurs as thin, translucent, greyish-white strips, or as yellowish, flattened bands, *insoluble* in cold water.

*Uses*. 1 in boiling water 200 forms on cooling a transparent jelly, suitable for invalids. It has little nutritive value—it is not digested—but is useful for treating constipation, especially of the type where the stools are hard and dry owing to complete absorption of liquid from the digestive tract. For this purpose it is best crushed into small pieces like bran—termed **Flaked Agar**. Clinical experience shows that finely-powdered or even sand-like powder is not efficacious. Teaspoonful doses occasionally of the dry substance in flake form sprinkled in a little moist food, e.g., stewed fruit, act as a mild aperient, softening the fæces, but should be employed at first in moderation, as it may possibly cause obstruction. By taking up moisture it increases the volume of the fæces and promotes peristalsis. It is used in the preparation of culture media for bacteria (*q.v.*).

**Chondrus** (*B.P.C.*). *Syn.* IRISH MOSS, CARRAGEEN (*Fr. Cx.*, *P. Ned. V, P. Belg. IV, P. Helv. V, P. Dan.*).

The dried sea-weed *Chondrus crispus* (Gigartinaceæ). It occurs as yellowish, translucent horny masses.

*Uses*. It is used in the form of a decoction as a demulcent in the treatment of coughs. Chondrus is also employed as an emulsifying agent and as a substitute for gelatin in the preparation of jellies for invalids.

**Decoctum Chondri (B.P.C.). Syn. MUCILAGO CHONDRI.**

**Dose.**—1 to 4 ounces (30 to 120 ml.) or more. 1 in 40. A useful emulsifying agent, especially when an homogeniser is available. Demulcent and nutritive; may be flavoured with sugar and lemon juice.

**Cydonia (B.P.C., P. Helv. V). Syn. QUINCE SEEDS.**

The seeds of *Pyrus Cydonia* (Rosaceæ), containing about 20% of mucilage (cydonin). One part of the seeds with 40 of water yields a thick jelly used as mucilaginous agent in toilet preparations. **Mucilage** of quince is official in some pharmacopœias, the strength varying from 1 in 25 to 1 in 100. The strength 1 in 25 of cold water or rose water is generally preferred. It is prepared by macerating with the cold water for from  $\frac{1}{2}$  to 2 hours, and straining without expression. **Decoction** of quince (1 in 80) is made by boiling for 10 minutes. A preservative is necessary.

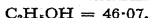
**Fucus (B.P.C.). Syn. BLADDER OR SEA WRACK, KELPWARE.** The dried plant, *Fucus vesiculosus* (Fucaceæ). Contains the gelatinous substance, algin, and a variable proportion, up to 0.2% of iodine. Was formerly used in goitre, obesity, and scrofula on account of its iodine content. It is recorded that a patient lost 20 lb. in weight in 9 weeks when taking the liquid extract, without bad results.

**Extractum Fuci (B.P.C.), dose**—3 to 10 grains (0.2 to 0.6 g.), is a soft extract prepared with alcohol 45%.

**Extractum Fuci Liquidum (B.P.C.).**

**Dose.**—1 to 2 drachms (4 to 8 ml.) before meals. 1 in 1.

**Adiposettes (Riddell Products, London).** Ext. fuc. vesic. 5.9%, Ext. frangul. 8%, lecithin 1%, tetraboryl-bis-propan-triolester 30%, triphenylcarbinol-o-carbonic acid glycolate 10%. Two to six tablets daily in obesity.

**ALCOHOL ÆTHYLICUM**

**Alcohol Dehydratum (B.P., U.S.P. XI, Fr. Cx., P.G. VI, P. Jap. V, P. Helv. V, P. Dan.). Syn. ALCOHOL ABSLUTUM.**

Ethyl hydroxide, with not more than 1% w/w of water. Sp. gr. 0.7936 to 0.7967 representing not less than 99.4% v/v or 99% w/w.

**Fr. Cx.**—Sp. gr. must not exceed 0.79683 at 15°. **P. Ned. V** allows 2% of water; **U.S.P. XI** sp. gr. 0.798.

**Antidotes (ACUTE POISONING).** Empty stomach by emetic or stomach tube. Keep patient warm, apply cold to head. Give 1 dr. of aromatic spirit of ammonia in 4 oz. of water, and a cupful of hot black coffee. Strychnine,  $\frac{1}{8}$  gr., hypodermically. Oxygen inhalations if necessary. Medicinal charcoal,  $\frac{1}{2}$  oz. in water, has been recommended.

**REFERENCE.** 10% carbon dioxide in oxygen administered with open slot mask; carbon dioxide increases respiratory excretion of alcohol, and oxygen will save life of rabbits given a dose of alcohol lethal to controls. Oxygen effective by speeding oxidation of alcohol rather than by relieving oxygen want. Clinically, results are encouraging; treatment recommended for acute alcoholism when danger of paralysis threatens life.—Robinson and Selesnick, *Lancet*, i/1936, 50.

**Alcohol (95%) (B.P.). Syn. ALCOHOL (U.S.P. XI, P. Helv. V, F.E. VIII), ALCOOL OFFICINAL or SPIRITUS RECTIFICATUS (Fr. Cx.), SPIRITUS RECTIFICATISSIMUS (P. Ital. V).**

Contains 94.7 to 95.2% v/v or 92.0 to 92.7% w/w of ethyl hydroxide. Sp. gr. 0.815 to 0.817.

**Alcohol (90%)** (*B.P., P. Jap. V.*). *Syn.* SPIRITUS RECTIFICATUS, SPIRITUS VINI (*P. Austr.*), SPIRITUS (*P. Ned. V, P. Helv. V.*).

Contains 89.6 to 90.5% *v/v* or about 85.7% *w/w* of ethyl hydroxide. Sp. gr. 0.832 to 0.835. Strength 57.80° O.P. (*i.e.*, 100 volumes contain approximately the same quantity of ethyl hydroxide as 157.8 volumes of proof spirit). It is generally manufactured commercially of higher alcoholic strength, *i.e.*, about 70 O.P., sp. gr. 0.809, containing nearly 95% *w/w* of ethyl hydroxide, and is diluted as required.

For various pharmaceutical purposes dilutions containing 70, 60, 45, 25 and 20% by volume are convenient. Alcohols of these strengths when required for official preparations may be prepared from alcohol (95%) by dilution with water, as described in the *B.P.*

*For Alcohol Dilution Tables see also Vol. II.*

**Alcohol Dilutum** (*U.S.P. XI*). Contains 41.5% *w/w* or 48.9% *v/v* of ethyl hydroxide.

*Note.*—*U.S.P. XI* orders on occasion a mixture of "Alcohol" 3 parts and water 1 part as menstruum in making tinctures and fluid-extracts. This is approximately equivalent to 70% by volume.

**Alcohol Dilutus** (*P. Jap. V*) is alcohol 60%.

**Proof Spirit.** *Syn.* SPIRITUS TENUIOR (*B.P. '85*).

Proof Spirit contains 49.28% *w/w* of ethyl alcohol, or at 60°F., 57.10% *v/v* of ethyl alcohol. Sp. gr. 0.91976. It was defined in the Spirits Act, 1815, as that spirit which at 51°F. weighed exactly  $\frac{1}{3}$  of an equal volume of distilled water. It may be prepared by mixing 5 volumes of rectified spirit (sp. gr. 0.838) with 3 volumes of distilled water.

The strength of alcohol is frequently stated in terms of proof spirit. Spirit of such a strength that 100 volumes contain as much ethyl alcohol as 160 volumes of proof spirit is described as "60 O.P." (over proof). Spirit of which 100 volumes contain as much alcohol as 40 volumes of proof spirit is described as "60 U.P." (under proof).

For the purposes of Customs and Excise the quantity of spirit is always expressed in proof gallons, obtained by adding 100 to the number of degrees "overproof." Hence it follows that the figure for the number of proof gallons is no direct indication of the volume of the spirit. For example: 100 gallons of 90% *v/v* alcohol ("57.8 O.P.") is equivalent to 157.8 proof gallons, while 100 gallons of 10% *v/v* alcohol ("82.47 U.P.") is equivalent to 17.53 proof gallons.

**Uses.** Alcohol administered internally is a depressant to the central nervous system, the apparently stimulating effect being due to early inhibitory action on the higher centres such as those controlling self-criticism and judgment. It stimulates the secretion of gastric juice, thus increasing appetite when taken before meals and improving digestion when taken during meals. Continued excessive dosage leads to chronic gastritis. Strong alcohol causes increase in the rate and strength of the heart beat, and the skin vessels are dilated, causing a sensation of warmth. It should not

be given to those in a cold atmosphere, since the vasodilatation and the depression of the heat-regulating centre cause a greater loss of heat. It is employed as a prompt reflex stimulant in fainting and collapse. In fevers, especially in acute pneumonia, it is valuable as a readily assimilated food, acting at the same time as a nerve sedative. Its food value is also useful in cases of diabetes when the diet must be restricted. Externally, alcohol is applied diluted in evaporating lotions in various superficial inflammations such as bruises, sprains, etc. Concentrated alcohol, *e.g.*, surgical spirit, is applied for the prevention of bed sores, for hardening the nipples prior to lactation, and as an anhidrotic. It is extensively used for sterilising the skin and instruments; the maximum bactericidal effect is exhibited by a 70% dilution; stronger solutions are less effective because less able to penetrate the bacterial cell. An injection of 15 m. of alcohol 80 or 90% into the Gasserian ganglion is of value in trigeminal neuralgia, owing to destruction of nerve tissue, but the relief is rarely more than temporary. Similar injections have been tried in other neuralgias and in sciatica, and it has been employed by intraspinal injection for the relief of pain in cancer. As a gargle or spray diluted alcohol is a useful local application in tonsillitis, pharyngitis and diphtheria.

A compress of alcohol applied on cotton-wool so as to cover the whole abdomen and covered with a cold-water compress and a layer of impermeable tissue, the cold water being renewed hourly, has been used in the treatment of typhoid fever, especially of children.

**ANÆSTHESIA.** *General anæsthesia* by alcohol in glucose solution. Two solutions are used: (a) Isotonic glucose solution, (b) 30 ml. of 96% ethyl alcohol in 70 ml. of 25% glucose solution. *Intravenous dose* is estimated according to patient's weight at 2 to 3 ml. of the 96% pure alcohol per kilo, but the maximum allowance is seldom exceeded. A few ml. of (a) is allowed to run in first. —J. D. Constantin, *Lancet*, i/1929, 1247, 1263; *ibid.*, i/1930, 1393.

**CANCER.** The subarachnoid injection of a mixture of 60% absolute ethyl alcohol and 40% absolute methyl alcohol is of value for the relief of intractable pain in advanced cancer. Puncture is performed in the interspace corresponding to the level of emergence from the cord of the nerves supplying the painful area, an amount of spinal fluid equivalent to the amount of alcohol to be injected being withdrawn. The head of the patient is kept at a lower level than the site of injection and the spine flexed to as acute an angle as possible at this point. 0.8 to 2.0 ml. of the alcohol mixture is injected slowly (at least 1 minute for each ml.). The patient is then kept as nearly as possible in the same position for 4 hours, then flat in bed for 12 hours, and confined to bed for several days. No serious complication, but preoperative administration of phenobarbital 0.2 g. and morphine 0.01 to 0.015 g. is of value. Visceral pain is less amenable than somatic pain. —J. E. Dunphy, *New Engl. J. Med.*, 1936, 214, 472.

The injection of sterile dehydrated alcohol in small doses is advocated for the relief of pain in chronic painful conditions such as cancer. A single subarachnoid injection usually gives relief for 10 to 12 months and obviates the need for large doses of narcotics. Excessive dosage may cause rectal and vesical incontinence. —E. L. Stern, *Med. Rec.*, N.Y., i/1936, 327.

The following procedure recommended for the relief of pain in the final stages of cancer of the bladder, prostate and rectum. Lumbar puncture is performed at the first lumbar interspace and 1 to 1.5 ml. of dehydrated alcohol injected slowly. The side on which pain is most severe is placed uppermost, the patient left in position for 10 minutes and then on his back with the foot of the bed raised for 3 hours. The second injection can be given a few weeks later or when necessary. —G. M. McKenna and E. Oldberg, per *Med. Annu.*, 1937, 56.

**NEURALGIA.** Intractable trigeminal neuralgia or tic douloureux has been treated by alcohol injections (80% usually employed). Injection of the nerve at the foramen ovale, or rotundum, relieves pain for at least a year, with injection of ganglion if neuralgia returns within 18 months.

**Trigeminal neuralgia.** Hartel injection route, using alcohol, into the region of the Gasserian ganglion.—L. Morris, *Lancet*, i/1931, 122.

Wilfred Harris now uses 2% Novocain to test cutaneous anaesthesia. Important to inject not more than 2 minims of alcohol at a time and test anaesthesia with a pin before injecting more. To correct commencing anaesthesia of the eye (causes "blinking") push needle another  $\frac{1}{4}$  inch into ganglion, but before injecting watch for cerebrospinal fluid—if this appears withdraw partly and reinsert in a more backward direction.—*Brit. med. J.*, ii/1932, 88.

**PROLAPSE OF RECTUM.** Injection treatment using absolute alcohol, 1.5 ml. being injected on each side into the perirectal tissues at a depth of 2 to 2 $\frac{1}{2}$  inches, the needle being inserted about a  $\frac{1}{4}$  inch from the anal margin. A pad is then placed in the perineum and kept in position by strapping the buttocks, the pad and strapping being reapplied daily for a week.—L. Findlay, *Brit. med. J.*, ii/1934, 340; H. Williamson, *ibid.*, 331.

**PRURITUS VULVÆ.** Successful results from alcohol injections in 41 cases (average duration 8 years) in which more conservative measures had failed. At one sitting, under general anaesthesia, from 2 to 4 minims of 95% alcohol were injected just beneath the dermis at each of a number of points at least 1.5 cm. apart. Oedema, thickening, and itching disappeared almost at once. 24 patients had enduring relief from one injection and in only two patients was the treatment completely ineffective.—W. M. Wilson, *J. Amer. med. Ass.*, i/1933, 493.

**SCIATIC NEURALGIA.** Alcohol injections recommended, but the small margin of safety demands strict adherence to proved technique.—C. W. Goff, *Amer. J. Surg.*, 1936, 37.

#### **Alcohol in Medicinal Preparations.**

The conditions under which alcohol may be obtained, used and sold are controlled through H.M. Customs and Excise. Two classes of spirit are recognised, Mature Spirit and Immature Spirit. The former is that which has been stored for at least three years in bond, the latter is that which has not been so stored, and which is used for the preparation of medicinal and other products. Both classes are subject to a duty which is payable at the time of purchase.

**Rebate.** When spirit on which the full duty has been paid is used in the preparation of medicinal products, the Customs and Excise will, under suitable conditions, allow a rebate. In order to claim the rebate, the manufacturer must comply with the official regulations, keeping a record of spirit purchased, how used, quantity of preparations produced, etc., in a register which must be open to inspection and balance by the Officers of the Customs and Excise. The claims for rebate are made to the local office of the Customs and Excise on a special form obtainable from them, and may be made once in every two weeks, but must not extend over a period longer than three months. Rebate is allowed on medicinal preparations such as Liq. Quinin. Ammon. B.P. or Tinct. Myrrhæ et Boracis B.P.C., but not on flavouring or colouring agents such as Tinct. Limonis B.P. or Tinct. Cocci B.P. Further, special permits are granted to draw rebate on formulæ which have been submitted to and approved by the Customs and Excise, provided the conditions of manufacture are complied with. The rebate claimed should be on the actual quantity of alcohol used in the manufacture of the preparation.

**Drawback.** For export purposes a drawback is allowed by the Customs and Excise equal to the amount of duty which has been paid on the spirit which is actually contained in the quantity of preparations exported. Claims for drawback must be made on official forms, and the various conditions imposed by the Customs and Excise must be complied with.

Further information on rebate and drawback can be obtained from the local Officer of Customs and Excise, who will advise inquirers of the conditions required.

**Duty Free Alcohol.** Under certain special conditions Immature Spirit can be obtained duty free for use where methylated spirit is unsuitable or detrimental, such as in the manufacture of esters, or for use by hospitals, schools, chemists, or other scientific workers for use in research or teaching. A bond must be given and the spirit must be denatured with 2% pure Methyl Alcohol in the presence of an officer of Customs and Excise in the place where it is to be used.



**Sale of Medicated Wines and Rectified Spirit.**

Although there is no statutory exemption permitting pharmacists to sell wines or spirits for medicinal use without an excise licence, in practice the Commissioners of Customs and Excise do not require an excise licence to be taken out by a person or limited company for the retail sale of medicated wines and sweets of the B.P., or other medicated wines and sweets or spirits which in the opinion of the Commissioners are sufficiently medicated to render them unsuitable as a beverage. The directions on the label as to dose, etc., must clearly indicate that the preparation is intended for use as a medicine. The Commissioners also allow the sale without licence of rectified spirit in quantities not exceeding 5 ounces at one time for medical purposes or scientific research.

[P2] **Alcohol Ammoniatum (B.P.C.).** A 10% *w/w* solution of ammonia gas in alcohol. Is used in the preparation of parogens.

**Lotio Evaporans (B.P.C.).** Alcohol, 1 in 8, with ammonium chloride and distilled water.

**Spiritus Frumenti.** Whisky prepared by distillation of fermented grain—barley, wheat, rye, Indian corn. Sp. gr. is usually about 0.925. It usually contains about 40% *v/v* of alcohol, 0.1 to 0.2% of higher alcohols, 0.03 to 0.08% of esters, 0.2 to 0.8% of volatile acid with traces of furfuraldehyde and other substances.

**U.S.P. XI**—From wholly or partly malted cereal grains and not less than four years old, 47–53% by vol.

**Spiritus Vini Gallici.** BRANDY. *Syn.* EAU DE VIE (*Fr. Cx.*). The liquid obtained by distillation of the wine of grapes and matured by age. Contains 40 to 50% (or 60% in case of good Cognac) by volume of alcohol. *P. Helv. V* requires a minimum of 50%, *Fr. Cx.* 45 to 55%, *P. Jap. V* 35 to 39%.

Contains about 0.05 to 0.15% of higher alcohols, 0.1 to 0.15% of esters, 0.05 to 0.2% of volatile acid with traces of furfural and other substances.

**Spiritus Vini Vitis (U.S.P. XI)** has 48 to 54% by vol., and is not less than 4 years old.

**Mistura Spiritus Vini Gallici (B.P.C.).**

*Dose.*—1 to 2 ounces (30 to 60 ml.), as a draught.

2 oz. contains about  $\frac{1}{2}$  oz. of brandy with yoke of egg, sugar and cinnamon water.

**Vinum Xericum (B.P.C.).** *Syn.* SHERRY-TYPE WINE.

Prepared by the fermentation of grape juice. It may be either true sherry, prepared only in Spain, or wine of a similar type prepared elsewhere; such as in Australia or South Africa. It contains not less than 16% *v/v* of alcohol.

**Vinum Xericum Detannatum (B.P.C.)** is sherry-type wine detannated with gelatin. It does not yield precipitates with alkaloidal solutions.

**Alcohol Allylicum.**  $\text{CH}_3\cdot\text{CH}_2\cdot\text{OH} = 58.05$ .

A colourless liquid miscible with water, with a pungent odour and burning taste. It inhibits bacterial growth.

Open chain derivatives containing unsaturated carbon atoms are more toxic than isomeric saturated bodies. Thus allyl alcohol is 50 times more toxic than normal propyl alcohol.

**ALCOHOL AMYLICUM**

*B.P.C.*

$\text{C}_5\text{H}_{11}\cdot\text{OH} = 88.15$ .

Obtained by purifying fusel oil, and consists of a mixture of about 90% of primary *iso*amyl alcohol,  $(\text{CH}_3)_2\text{CH}\cdot\text{CH}_2\cdot\text{CH}_2\text{OH}$ , and 10% of primary active amyl alcohol,  $\text{CH}_3\cdot\text{CH}_2\cdot\text{CH}(\text{CH}_3)\cdot\text{CH}_2\text{OH}$ . Occurs as a colourless liquid with characteristic odour. B.p.  $128^\circ$  to  $132^\circ$ . Sp. gr. 0.815 to 0.817.

**Soluble** slightly in water; miscible with fixed and volatile oils and with alcohol, ether, chloroform and other organic liquids.

**Amylis Acetas** (*B.P.C.*).  $\text{CH}_3\cdot\text{COOC}_5\text{H}_{11}$ . A colourless, inflammable liquid with a powerful, pear-like odour. Very slightly **soluble** in water, miscible with ether, alcohol 90% and other organic liquids.

[P.] **Amylis Nitris** (*B.P., U.S.P. XI, etc.*). *Syn.* AMYLIUM NITROSUM, AZOTITE D'AMYLE.  $\text{C}_5\text{H}_{11}\text{NO}_2 = 117\cdot15$ .

**Dose.**—By inhalation, the vapour of 2 to 5 minims (0·12 to 0·3 ml.); up to 10 minims may be inhaled. Very rarely it has been given by the mouth in doses of  $\frac{1}{2}$  to 1 minim (0·03 to 0·06 ml.), or hypodermically in doses of 1 to 5 minims (0·06 to 0·3 ml.).

A yellowish ethereal liquid with a peculiar, not disagreeable odour; produced by the action of nitrous acid on amylic alcohol boiling between  $128^\circ$  and  $132^\circ$ , and consists chiefly of the nitrites of isobutylcarbinol,  $(\text{CH}_3)_2\text{CH}\cdot\text{CH}_2\cdot\text{CH}_2\text{OH}$ , and *sec.*-butylcarbinol  $(\text{C}_2\text{H}_5)(\text{CH}_3)\text{CH}\cdot\text{CH}_2\text{OH}$ . Should be kept cool; on exposure to the air it becomes comparatively inert.

**Insoluble** in water; miscible with alcohol and ether.

Thin glass capsules, encased in cotton-wool and silk, are made containing usually 3 minims, also 1, 2, 4, 5, 6 or 10 minims.

In use the capsule is broken, the liquid soaks the cotton-wool, and the vapour can be inhaled.

**Incompatible** with alkaline carbonates, potassium iodide, bromides and ferrous salts.

**Antidotes.** Empty stomach by emetic (if amyl nitrite has been swallowed). Keep patient lying down and warm. Apply artificial respiration if necessary and give inhalations of oxygen, alone or with 5% carbon dioxide. Injections of adrenaline or ephedrine.

**Pharmacology.** Amyl nitrite dilates the vessels and lowers blood-pressure. The vessels of the head and neck are most affected, and within 30 to 40 seconds after inhalation or swallowing a dose, the face flushes, the heart beats become rapid and violent, and the head and neck perspire. The effect on the pulse can be shown within 10 seconds of inhalation, but lasts usually for 2 to 3 minutes only. The rapidity of action is due to the large area of the lungs absorbing the drug—roughly 100 sq. metres—and to the thinness of the membranes (about  $\frac{1}{1000}$  mm.) separating the air of the pulmonary vesicles from the blood.

**Uses.** It is mainly used for the relief of attacks of angina pectoris, acting by dilatation of the coronary artery. Its use is contraindicated in coronary thrombosis. In chloroform syncope amyl nitrite affords the quickest means of restoring the heart's action. It may be used in status epilepticus, and will frequently abort an epileptic fit if inhaled during the aura of an attack. Hæmoptysis can in most cases be immediately arrested if amyl nitrite is inhaled as soon as the first signs of blood are seen in the sputum. It is also valuable in cerebral and in post-partum hæmorrhage, and may be used to control menstrual flooding, *e.g.*, in tiding over fibroid disease until the menopause. It may also be used in migraine and neuralgic dysmenorrhœa and in the spasms of tetanus, false croup, whooping cough and strychnine poisoning. Inhalation of 1 minim may be used in infantile convulsions and

may cut short the attack. It is a powerful agent for causing relaxation of uterine spasms and hour-glass contraction, whether natural or caused by ergot; spasm of the bile duct during passage of a calculus may also be relieved by the inhalations. Externally amyl nitrite 10% in alcohol 90% has been applied to the scalp on alternate nights to assist the action of stimulant hair lotions such as pilocarpine hair lotion. Local application supplemented by inhalation has been used successfully in the treatment of urticaria, eczema and other skin diseases.

**ANGINA PECTORIS.** Observations upon angina pectoris. Nature and distribution of the pain, duration of attack, ætiology—the current theory is that it results from muscular anoxæmia—diagnosis, prognosis, treatment. If the blood pressure is raised during attacks the nitrites are useful, but useless if it is not raised.—John Cowan, *Brit. med. J.*, i/1931, 879.

No reason why amyl nitrite and nitroglycerin should not be used indefinitely. They enable patient to lead a more normal life.—Maurice Campbell, *Practitioner*, i/1931, 35.

**AORTIC INCOMPETENCE** of syphilitic origin. Amyl nitrite gave almost instant relief of pain.—C. F. Coombs, *Brit. med. J.*, i/1928, 1012.

**UTERINE SPASM.** In cases of "contraction ring" amyl nitrite inhalation is the one method of treatment which alone seems to meet with universal success. Description of 5 cases, inhalation followed by delivery.—C. R. Croft, *Lancet*, ii/1928, 167.

**VOMITING OF PREGNANCY.** Spasm of the duodenum occurs in some cases of vomiting of pregnancy. In such cases relief may be obtained by inhalation of amyl nitrite or by administration of glyceryl trinitrate  $\frac{1}{10}$  grain placed under the tongue 3 times daily.—J. M. McGowan *et al.*, *J. Amer. med. Ass.*, i/1938, 498.

**Amyleni Hydras** (*B.P. Add. III, P. Helv. V; P. Ned. V, P.G. VI*). *Syn.* DIMETHYL-ETHYL CARBINOL, TERTIARY AMYL ALCOHOL.  $(CH_3)_2C_2H_5C\cdot OH = 60.09$ .

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.). The Continental pharmacopœias have maximum single dose 1 dr. approx., maximum in 24 hours 2 dr. May be given in capsules or in a mixture flavoured with liquorice.

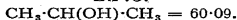
A colourless liquid, of pungent taste and odour, resembling a mixture of paraldehyde and camphor.

**Soluble** in 8 of water; miscible with alcohol 90%, ether, chloroform and glycerin.

**Uses.** Hypnotic, occupying a position between chloral and paraldehyde; a stage of excitement may precede hypnosis. Capsules contain 10 minims in each. It is used as a solvent for tribromoethylalcohol in bromethol (*see p.* 316).

## ALCOHOL ISOPROPYLICUM

*B.P.C.*



*Syn. and Prop. Name.* SECONDARY PROPYL ALCOHOL, DIMETHYL CARBINOL, AVANTINE (*Howards & Sons, Ilford*).

**Isopropyl Alcohol Regulations, 1927.**

*Manufacturers, sellers and users of Isopropyl Alcohol in Great Britain and Northern Ireland must render returns to the Customs*

*and Excise authorities, showing the quantity manufactured, used, and/or sold, together with the names of purchasers, and the purposes for which the Alcohol has been used.*

A colourless liquid with spirituous odour and somewhat burning taste, containing about 96% *v/v* (94% *w/w*) of  $C_3H_8O$ . Sp. gr. 0.808 to 0.810; b.p. 80.5° to 82.2° (B.P.C. gives sp. gr. 0.810 to 0.812, b.p. 80.5° to 81.5°). It is also obtainable containing 98 to 99% *w/w*, with sp. gr. 0.793 to 0.795 and b.p. 81.5° to 82.4°. In the anhydrous condition it has sp. gr. 0.788 and b.p. 82.4°. It is miscible with water or ethyl alcohol in all proportions.

**Preparation.** It may be made synthetically, *e.g.*, by reducing acetone, using sodium amalgam or by passing acetone and hydrogen over a metallic catalyst. It is also obtained from propylene, a by-product of the petroleum industry in the U.S.A., by absorbing the olefine gases, containing propylene, in sulphuric acid and hydrolysing the resulting alkylsulphuric acids.

The rectified product contains 91% of the alcohol; with dry caustic soda it can be made anhydrous.

**Pharmacology.** Isopropyl alcohol is twice as toxic as ethyl alcohol intravenously in cats. Vapour of isopropyl alcohol did not kill rats exposed to fumes (*cf.* methyl alcohol). 50 ml. given *per os* to a dog weighing 6.5 kilo. caused serious incoordination, but the animal completely recovered. Applied to wounds in concentration up to 50% allowed same to heal normally.

It is stated to be less toxic than *n*-propyl alcohol. Administration by mouth produces narcosis, in larger doses anæsthesia, finally coma and death. Very little is absorbed by inhalation or through the skin.

**Uses.** It is safe internally in small doses in dilute form, and could be used for making tinctures of drugs. It has been suggested as a surgical antiseptic and could, no doubt, replace ethyl alcohol in many surgical and medical procedures. In commerce, it is also suitable as a solvent for crystallising and for extract manufacture. It is now largely used in perfumery and in the culinary arts (flavouring essences). *Externally*, it has been found harmless to the skin and hair, and within reason it can be inhaled mixed with air.

*The above remarks apply, it should be noted, to isopropyl alcohol. The isomeric NORMAL, OR PRIMARY, PROPYL ALCOHOL,  $CH_3 \cdot CH_2 \cdot CH_2 \cdot OH$ , is more toxic and unsuitable for making tinctures and the like.*

## ALCOHOL METHYLICUM

B.P.C.

$CH_3 \cdot OH = 32.04$ .

Syn. METHANOL.

**Dose.**—30 to 60 minims (2 to 4 ml.).

Methyl alcohol is synthesised on a commercial scale from water gas (a mixture of carbon monoxide and hydrogen) under pressure at about 400° in presence of a catalyst, usually metallic copper containing 10% of zinc oxide.

Synthetic methyl alcohol has been used as an anti-freeze mixture for radiators. Toxic effects in U.S.A.—*Brit. med. J.*, ii/1930, 745.

If absolute and "acetone-free," methyl alcohol has sp. gr. 0.796, but it is not allowed by the Excise to be retailed pure unless duty-paid. *B.P.C.* requires the sp. gr. to be not higher than 0.799. The commercial substance known as WOOD NAPHTHA, PYROXYLIC SPIRIT, or WOOD SPIRIT, is 60 to 90% pure, and contains acetone and other empyreumatic impurities. The variety used for denaturing alcohol contains 72% *v/v* of methyl alcohol. It is a solvent of pyroxylin. The methylated spirit licence is not necessary for the sale of wood spirit, but that licence does not, of course, cover the sale of pure methyl alcohol.

**Antidotes.** Empty stomach by emetic or by stomach tube, using 5% sodium bicarbonate solution. Give water freely. Keep patient warm. Strychnine,  $\frac{1}{2}$  gr., hypodermically.

**Methylated Spirits.** Four varieties of methylated spirits are recognised. Mineralised Methylated Spirits, Industrial Methylated Spirits, Industrial Methylated Spirits (Pyridinised) and Power Methylated Spirits. Mineralised Methylated Spirits consists of alcohol mixed with wood naphtha (9.5%) and crude pyridine (0.5%). To every 100 gallons of the mixture is added  $\frac{1}{4}$  of a gallon of mineral naphtha (petroleum oil) and not less than  $\frac{1}{4}$  of an ounce of methyl violet. It forms an opaque mixture with water.

**Caution.** Mineralised Methylated Spirits is not well adapted for local use, *e.g.*, for bed sores. It caused dermatitis amongst surgeons of Manchester Royal Infirmary, and among barbers of that city. Pyridine, added to render the spirits undrinkable, was probably the cause of the trouble.

Industrial Methylated Spirit consists of alcohol containing 5% of wood naphtha. Its use is permitted in the preparation of a number of *B.P.* and *B.P.C.* formulæ, in the articles specified in the *N.P.U.* formulary, and in special formulæ which have been approved by the Customs and Excise authorities.

**Spiritus Methylatus Industrialis (B.P.).** *Syn.* SPT. ANTI-SEPTICUS (*N.I.F.*); INDUSTROL (*N.I.F.*). Industrial methylated spirit, *B.P.*, is a mixture of 19 parts of alcohol (95%) and 1 part of wood naphtha, and is of the quality known as 66 O.P. industrial methylated spirits. It is, therefore, considerably purer than the mineralised spirit and of greater utility for manufacturing purposes.

**Spiritus Methylatus Industrialis sine Acetono (B.P.C.).** INDUSTRIAL METHYLATED SPIRIT (ACETONE-FREE).

Is of the same strength as industrial methylated spirit, *B.P.*, but the denaturant used is practically free from acetone. It is compatible with iodine, with which industrial methylated spirit containing acetone yields irritating vapours.

**Spiritus Chirurgicalis (B.P.C.).** SURGICAL SPIRIT.

Formula No. 1 contains industrial methylated spirit with castor oil, methyl salicylate and ethyl phthalate. Formula No. 2 contains

industrial methylated spirit with castor oil, mineral naphtha and ethyl phthalate.

These are the only formulæ which are at present approved by the Board of Customs and Excise, and there are no restrictions on purchase or sale by chemists. Surgical spirit made to any other formula may be supplied on prescription only; it cannot be purchased from the wholesaler but must be made by the chemist as required, and is subject to the statutory regulations relating to dispensing prescriptions for preparations containing I.M.S.

When surgical spirit is ordered on a *N.H.I.* prescription, No. 2 formula must be dispensed unless the prescription directs otherwise.

Surgical spirit may not be used as a base in the manufacture of other preparations. It must be sold exactly as received from a wholesaler.—*Pharm. J.*, i/1926, 323, 536.

**Methylated Spirit Drinking.** Methyl alcohol is capable of producing an intoxication similar to that caused by ethyl alcohol but distinct in the slowness of the onset and the extraordinary duration of the symptoms which may last from 3 to 4 days after taking a comparatively moderate dose. The symptoms observed are a marked fall of body temperature, convulsions, vomiting, dilatation of the pupils, and nystagmus. Characteristic of the poisoning is the loss of vision which begins generally within 24 hours and may progress to complete blindness, and permanent blindness has even followed the inhalation of the fumes by workmen engaged in industrial processes. The fatal dose is comparatively small and death has been reported from the drinking of less than 30 ml. In 1926 two thousand people died in America as a result of drinking so-called whisky prepared from denatured alcohol. Some years ago in the poorer quarters of London and Glasgow the drinking of a mixture of methylated spirits and cheap red wine constituted a matter of serious concern to the authorities. The mixture, which was obtainable at ninepence a quart bottle, was popularly known as "Red Lizzie" or "Red Biddie." It was said that a man or woman taken when under the influence of this drink might be unconscious for 24 hours, and at the end of that period if they took a drink of water or any other liquid they immediately became drunk again.

### ***Methylated Spirits Regulations.***

The regulations governing the use of Methylated Spirits have been revised and consolidated by the Methylated Spirits Regulations, S.R. & O., 1930, No. 832, amended by the Methylated Spirits (Amendment) Regulations S.R. & O., 1934, No. 1139, and amplified by Notices issued by the Commissioners of Customs and Excise. Methylated spirits must not be purified and must not be recovered or redistilled, except by sanction of the Commissioners. Any methylated spirits or spirits so recovered or redistilled shall be kept under the control of the user, or under lock or otherwise to the satisfaction of the proper officer. Bottles or other containers holding articles made with Industrial Methylated Spirit for medical purposes and put up for sale or supply must be labelled "For External Use Only," "Not To Be Taken" or otherwise to the same effect. The following are among the other conditions governing the sale of mineralised and industrial methylated spirits.

**Mineralised Methylated Spirits.** Only mineralised methylated spirits may be sold by retail for general use, and every retailer must obtain a Customs and Excise licence, renewable annually, at a cost of 10/-. A chemist, upon application for a licence, must notify the local officer of Customs and Excise of the premises he intends to use in connection with the storage and sale of spirits.

A licensed retailer may not hold in stock more than 200 gallons and he may neither buy more than 4 gallons from another retailer nor sell more than 4 gallons to any one person at one time. Mineralised methylated spirits may not be sold between 10 p.m. on Saturday and 8 a.m. on Monday.

#### **Industrial Methylated Spirit.**

A. Sale for medical and scientific purposes by wholesale chemists and dispensing chemists (NOTICE No. 53).

(1) Any wholesale or dispensing chemist with a Methylated Spirits Retailer's Licence may, on application, receive Industrial Methylated Spirit in quantities *not exceeding 4 gallons* for sale to authorised users on receipt of requisition in the *official form*. This applies to *all* sales of Industrial M.S. to dispensing chemists, and the limit of 1 gallon is now *withdrawn*.

May be sold in quantities *not exceeding  $\frac{1}{2}$  gallon* at a time to a medical practitioner, dentist, veterinary surgeon, hospital or nursing home, on a *signed order*—purchaser *need not hold official authority* or submit a requisition, but order must be signed by a doctor, chemist, or veterinary surgeon. This does *not* cover supplies to dispensing chemists.

(2) Industrial M.S. may be exported in quantities *not exceeding 4 gallons*. Requisitions unnecessary, and the spirits may be supplied merely on customer's order.

(3) Every wholesale or dispensing chemist wishing to sell Industrial M.S. must apply for special authority, *whatever authority he may already hold*.

(4) Regn. 50 requires Industrial M.S. for sale in accordance with para. (1) and (2) to be kept apart from I.M.S. used for other purposes, a separate stock being kept under proper control, and an account kept of this separate stock. Accounts must be balanced monthly, orders and documents must be kept for two years and the contents of bottles or other containers must be labelled "Industrial Methylated Spirits."

#### **B. Dispensing chemists (NOTICE No. 54):**

1. Where already authorised to receive Industrial M.S. for dispensing, he is automatically and without further application entitled to use and dispense I.M.S. as at (i) and (ii) para. 2, while being liable to conditions in para. 3 and 4. If existing authority covers use of I.M.S. in making articles not in Second Schedule he will continue to be entitled to use I.M.S., but as from Jan. 1, 1931 no authority held prior to that date to sell I.M.S. to other chemists is valid, and special authority must be obtained.

2. All future applications must be made on special form (Ex. No. 225A), and grant of authority will convey (i) right to make and sell articles in Second Schedule; (ii) right to make and dispense on prescription only articles not scheduled or authorised, or I.M.S. subject to Regulations and Conditions in para. 4. Application may also include request for authority to use I.M.S. in making other articles or for other specified purposes.

3. Permits received from methylators must be kept and delivered to Officer. M.S. must not be purified, except with special sanction. M.S. must be kept under proper control. All containers to be labelled "For external use only," or "Not to be taken," or otherwise to the same effect. Return to be made once a year.

4. Articles not in the Second Schedule or authorised may be supplied only on the following conditions:—

- (i) Dispensed only on signed order or prescription by medical practitioner, dentist, or veterinary surgeon.
- (ii) A prescription or order for I.M.S. diluted or undiluted must specify the quantity required, must not be acted on more than once, or more than 7 days after date borne, and, unless issued under N.H.I. must be kept for two years.
- (iii) Articles made with I.M.S. on prescription *not* issued under N.H.I. must be entered in Prescription Book with name of person for whom prescription is written and person by whom signed. Prescriptions according to formulae given in any recognised book of reference may be quoted by the recognised short title.
- (iv) Not more than 1 pint of I.M.S. alone, or diluted, or as an ingredient may be supplied at one time to any one person.
- (v) Containers to be labelled.

The Second Schedule to the Regulations, 1930, as amended by the Regulations, 1934, includes articles in the *B.P.*, *B.P.C.*, *N.I.F.*, and *N.P.U. Formulary* for external use only, *B.P.* and *B.P.C.* preparations made with alcohol providing

no spirit remain in the finished product, *B.P.* and *B.P.C.* reagents, and paint and varnish thinners.

C. Regulations concerning doctors, dentists, veterinary surgeons, hospitals, and nursing homes (NOTICE NO. 54).

1. Medical men, etc., may obtain authority to receive I.M.S.
2. I.M.S. (95% Ethyl Alcohol denatured with 5% Wood Naphtha) may be had in various strengths, including a strength corresponding to absolute Alcohol.
3. From a methylator not less than 5 gallons, or from an authorised wholesale or dispensing chemist not more than 4 gallons, may be obtained at one time, and official requisition must be sent.
4. Without authority he may obtain  $\frac{1}{2}$  gallon from a chemist.
5. I.M.S. may be used for dispensing or be used without admixture for any medical, etc., purposes *only*.
6. Must be labelled "For external use," or "Not to be taken," or words to that effect.

Only 1 pint may be dispensed by a medical man, etc., either alone or as an ingredient, at one time for any one person.

#### French Polish or Finish (Spirit Varnish).

Industrial M.S., providing special authority is obtained from the Commissioners of Customs and Excise, may be used in making for sale: (a) Mixtures containing not less than 8 ounces of resin (or 6 ounces of commercial shellac) to the gallon, (b) hot lacquers, irrespective of the proportion of resin (if not less than 3 ounces).

Mineralised M.S. may be used in making **Finish** for which the minimum of 3 ounces of gum resin is required.

Mixtures (except hot lacquers) containing 3 ounces or more but less than 8 ounces (or 6 ounces if the resin is commercial shellac) to the gallon, must, if for sale, be made with I.M.S. (Pyridinised).

**The Retailing of Mineralised Methylated Spirits and Surgical Spirit in Scotland** is controlled by the Methylated Spirits (Sale by Retail) (Scotland) Act, 1937, and a summary is given of the restrictions so far as they relate to authorised sellers of poisons in Scotland.

Mineralised methylated spirits and surgical spirits may only be sold on premises registered under the Pharmacy and Poisons Act, 1933. Containers must be labelled with the name of the seller, the address of the premises from which the sale is made and the words "methylated spirits" or "surgical spirit" as the case may be. Prior to delivery the seller must either enter in a book the date of the sale, the name and address of the purchaser, the name and quantity of spirits sold and the purpose for which it is required, and obtain the signature of the purchaser, or he must receive a signed order specifying the address of the purchaser, the name and quantity of spirits required and the purpose for which it is required. He must be satisfied that the signature is genuine and must make the same records as for a sale over the counter, entering in the place reserved for the signature of the purchaser the words "Signed Order." No time limit is specified for the preservation of records and there is no requirement to retain signed orders for inspection.

*It is an offence to sell by retail methylated spirits or surgical spirit to any person under the age of fourteen.*

**Alternative procedure for surgical spirit.** The container must be distinctly labelled with the name and address of the person by whom it is supplied or dispensed, and the following particulars must be entered in a book used regularly but not exclusively for the purpose. In the case of sales on the prescription of a doctor, dentist or veterinary surgeon, the date dispensed, the quantity supplied, the name or initials and, if known, the address of the prescriber, the name and, if known, the address of the person to whom, and the date on which, the prescription was given, must be recorded, or in the case of sales without a prescription, the date, the quantity and the name of the person to whom supplied. In the case of repeat prescriptions for surgical spirit it is sufficient to record the date and quantity supplied, together with a reference to a previous entry recording the dispensing of the spirit. The requirements need not be satisfied in the case of N.H.I. prescriptions for surgical spirit.



## ALLIUM

*B.P.C., Fr. Cx.*

*Dose.*— $\frac{1}{2}$  to 2 drachms (2 to 8 g.).

The fresh bulb of *Allium sativum* (Liliaceæ). Garlic has a very strong and disagreeable odour; the taste is strongly pungent and persistent.

*Uses.* Preparations have been given in pulmonary phthisis, bronchiectasis, chronic bronchitis, gangrene of the lung, and whooping cough.

Laryngeal tuberculosis has been treated by  $\frac{1}{2}$  to 1 drachm, 2 or 3 times a day, of the juice, with Tinct. Lavand. Co. and Syrup. Simplex, also gargle or spray (or combined), accompanied by poultice (or blister) of pulped garlic externally—latter also to tuberculous ulcers. Fresh juice is not so severe in action as the pulped garlic. The juice should never be applied to broken surfaces. Lengthy application of poultices (3 to 4 weeks with changes) may be required, but effect should first be tried for a few hours, as some are more susceptible than others.

For lupus, apply the fresh juice at night and allow to dry; wash off in morning and apply a bland ointment.

Suppuration of wounds may be controlled by the juice diluted with 3 or 4 parts of water, a 1 in 10 dilution being used later when the suppuration is definitely controlled.

An inhalation of fresh garlic juice is also useful in pulmonary tuberculosis. The following solution may be used:—fresh garlic juice 56, alcohol (90%) 7, oil of *Eucalyptus citriodora* 1. Four ounces is sufficient for 3 weeks' treatment. The juice is *fresh* and *not filtered*. Patient to use the inhalation in a respirator at least 1 hour night and morning.

**Succus Allii** (*B.P.C.*).

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

The expressed juice preserved by the addition of alcohol.

**Syrupus Allii** (*B.P.C.*).

*Dose.*— $\frac{1}{2}$  to 2 drachms (2 to 8 ml.).

Contains about 18% *v/v* of the juice.

**Tinctura Allii** (*Fr. Cx.*). Prepared by maceration with alcohol 60%, using 1 of drug to 5 of menstruum.

**Allisatin** (*Sandoz, London*). Tablets of garlic and activated charcoal for intestinal affections, etc.

**Allium Cepa**, the ordinary onion, is of less strength than *Allium sativum*. *Hydrarthrosis* has been cured by placing the fleshy scales of the onion round the joint and keeping in place with a bandage.

**Oleum Allii Essentiale**. This oil is excreted through the lungs and skin—not apparently by the kidney. Its principal constituent is usually taken to be allyl sulphide. Stimulant, expectorant and stomachic. In chronic bronchitis, pneumonia, also in cholera and tuberculosis. *Dose* of either the natural oil or allyl sulphide,  $\frac{1}{2}$  to 2 minims, in capsules.  $\frac{1}{2}$  minim of allyl sulphide per kilo weight may be taken as lethal dose.

**Allylis Sulphidum** (*B.P.C.*). ( $C_3H_5S$ )<sub>2</sub> = 114.2.

*Dose.*— $\frac{1}{2}$  to 2 minims (0.03 to 0.12 ml.).

A colourless or yellowish oil with a garlic-like odour. B.p. about 138°, sp. gr. 0.890 to 0.900.

Slightly **soluble** in water; soluble in alcohol and ether.

**Uses.** Allyl sulphide when taken orally is excreted by the lungs and skin, and is employed for its bactericidal action in the treatment of pulmonary tuberculosis, for which purpose it is taken diluted with oil in capsules or by inhalation from an oronasal inhaler. Its use diminishes cough and expectoration and it is said to be of value in chronic bronchitis and bronchiectasis. It should not be given undiluted.

Externally it has been used in lupus and tuberculous abscesses.

## ALOE

*B.P., U.S.P. XI.*

**Dose.**—2 to 5 grains (0.12 to 0.3 g.). *U.S.P. XI* average dose 4 gr.

Aloes is the solid residue obtained by evaporation of the liquid which drains from the cut leaves of various species of *Aloe* (Liliaceæ). Four varieties are official in the B.P., namely: Cape aloes (*A. Ferox*), Curaçao aloes (*A. vera* var. *officinalis*), which was formerly produced on the island of Barbadoes and is still frequently called Barbadoes aloes, Socotrine and Zanzibar aloes (*A. Perryi*). *Aloe* (*Fr. Cx.*, *P. Ital. V*, *F.E. VIII* (Acibar) and *P. Jap. V*) is from various sources; *P. Belg. IV* and *P. Helv.* specify *A. ferox*; *P. Dan.* includes *A. ferox* and other species.

Cape aloes occurs in dark brown, glassy masses with a vitreous fracture and a characteristic odour. It is mostly used for veterinary purposes. Curaçao aloes occurs as dark, chocolate-brown, opaque masses with a dull waxy fracture, Socotrine aloes as nearly black opaque masses with a porous fracture and a pleasant cheesy odour, and Zanzibar aloes as livery-brown masses with a nearly smooth fracture and a slight odour. Cape and Curaçao aloes are almost entirely soluble in alcohol 60%.

**Uses.** Aloes and aloin act chiefly on the lower bowel. They are employed with soap, with iron and with strychnine in the treatment of habitual constipation. Aloes, in dose of 10 grains a day, is very unsafe for pregnant women, since it is likely to produce abortion.

### **Decoctum Aloes Compositum (B.P.C.).**

**Dose.**— $\frac{1}{2}$  to 2 ounces (15 to 60 ml.).

A 1% solution of aloes, with myrrh, potassium carbonate, liquorice and compound tincture of cardamom.

### **Decoctum Aloes Compositum Concentratum (B.P.C.).**

**Dose.**—1 to 4 drachms (4 to 16 ml.).

Diluted with 3 parts of water it yields a preparation of about the same strength as compound decoction of aloes.

**Extractum Aloes (B.P.C., P. Jap. V).**

*Dose.*—1 to 4 grains (0.06 to 0.25 g.).

The dried aqueous extractive.

**Pilula Aloes (B.P.).**

*Dose.*—4 to 8 grains (0.25 to 0.5 g.).

Contains aloes 58%, and hard soap, 29%.

**Pilulæ Aloes (U.S.P. XI).** *Average dose.*—2 pills.

Each pill contains 2 grains of aloes and 2 grains of hard soap.

**Pilula Aloes et Asafœtidæ (B.P.).**

*Dose.*—4 to 8 grains (0.25 to 0.5 g.).

Contains 30% each of aloes, asafetida and hard soap.

**Pilula Aloes et Ferri (B.P.).**

*Dose.*—4 to 8 grains (0.25 to 0.5 g.).

Contains exsiccated ferrous sulphate 10% and aloes 20%, with cinnamon, cardamom and ginger.

**Pilulæ Aloes et Myrrhæ (B.P.C.).** *Syn.* PILULÆ RUFI.

*Dose.*—1 or 2 pills.

Contain aloes 2 gr. and myrrh 1 gr.

[P1-81] **Pilulæ Aloes et Nucis Vomicae (B.P.C.).**

*Dose.*—1 pill.

Contain aloes 2 gr., dry extract of nux vomica  $\frac{1}{2}$  gr., and dry extract of belladonna  $\frac{1}{2}$  gr.

**Pulvis Aloes et Canellæ (B.P.C.).** *Syn.* HIERA PICRA.

*Dose.*—3 to 10 grains (0.2 to 0.6 g.).

Aloes 4, canella 1.

**Tinctura Aloes (B.P.C.).**

*Dose.*— $\frac{1}{2}$  to 2 drachms (2 to 8 ml.). Aloes 1 in 40, and liquid extract of liquorice.

Tampons saturated with this give relief in pruritus vulvæ.

**Tinctura Aloes Composita (B.P.C.).**

*Dose.*—1 to 2 drachms (4 to 8 ml.).

Aloes, about 1 in 30, with gentian, rhubarb and ginger.

**Tinctura Aloes et Myrrhæ (B.P.C.).** *Syn.* ELIXIR PROPRIETATIS.

*Dose.*—1 to 2 drachms (4 to 8 ml.).

Aloes about 1 in 10, with saffron, in tincture of myrrh.

[P1] **Tinctura Antiperiodica (B.P.C.).** *Syn.* WARBURG'S TINCTURE.

*Dose.*—1 to 4 drachms (4 to 16 ml.).

Contains aloes 1 in 40, quinine sulphate 1 in 50, with opium (0.03%) and 15 other drugs.

**Vinum Aloes (B.P.C.).**

*Dose.*—1 to 2 drachms (4 to 8 ml.).

Aloes about 1 in 30, with cardamom, in sherry-type wine.

**Aloinum (B.P., U.S.P. XI).**

*Dose.*— $\frac{1}{2}$  to 2 grains (0.03 to 0.12 g.).  $\frac{1}{2}$  grain may be considered an aperient, and 1 grain a full purgative dose. The former is U.S.P. XI average dose.

A mixture of crystalline principles from aloes. Usually obtained from Curaçao aloes and then contains approximately equal proportions of barbaloin (C<sub>21</sub>H<sub>20</sub>O<sub>9</sub>) and isobarbaloin.

**Soluble** about 1 in 130 of water, 1 in 20 of alcohol 90%. Almost insoluble in ether, chloroform and benzene.

Administered in a pill with hard soap. Assuming aloes to contain 25% of aloin, it follows that  $\frac{1}{4}$  grain of the latter is equivalent in activity to 1 grain of aloes.

Has been tried as *hypodermic purgative*— $\frac{1}{2}$  grain in warm water 30 minims, but it is not always satisfactory.

[P1-S1] **Pilulæ Aloini Compositæ** (B.P.C.). *Syn.* ANDREW CLARK'S LIVER PILLS.

*Dose.*—1 pill.

Contain  $\frac{1}{2}$  gr. each of aloin, dry extract of nux vomica, exsiccated ferrous sulphate, myrrh and hard soap.

[P1-S1] **Pilulæ Aloini et Podophyllini Compositæ** (B.P.C.).

*Dose.*—1 to 4 pills.

Aloin  $\frac{1}{10}$  gr., jalap resin  $\frac{1}{10}$  gr. and resin of podophyllum  $\frac{1}{2}$  gr., with oleoresin of capsicum and dry extracts of nux vomica and hyoscyamus.

[P1-S1] **Pilulæ Aloini et Strychninæ Compositæ** (B.P.C.).

*Dose.*—1 or 2 pills.

Aloin  $\frac{1}{2}$  gr., strychnine  $\frac{1}{80}$  gr. with dry extract of belladonna and powdered ipecacuanha.

[P1-S1] **Pilulæ Phenolphthaleini Compositæ** (B.P.C.). *Syn.* PILULÆ PHENALOINI.

*Dose.*—1 or 2 pills.

Aloin  $\frac{1}{2}$  gr., phenolphthalein  $\frac{1}{2}$  gr., strychnine  $\frac{1}{80}$  gr., dry extract of belladonna  $\frac{1}{12}$  gr., powdered ipecacuanha  $\frac{1}{15}$  gr.

**Tabellæ Aloini** (B.P.C.) contain  $\frac{1}{2}$  gr. (0.03 g.).

[P1-S1] **Tabellæ Aloini Compositæ** (B.P.C.).

*Dose.*—1 or 2 tablets.

Aloin  $\frac{1}{2}$  gr., powdered ipecacuanha  $\frac{1}{2}$  gr. and dry extract of nux vomica  $\frac{1}{2}$  gr.

[P1-S1] **Allophen Pill** (Parke, Davis, London). Aloin,  $\frac{1}{2}$  gr., phenolphthalein  $\frac{1}{2}$  gr., ipecacuanha  $\frac{1}{15}$  gr., strychnine  $\frac{1}{120}$  gr., and extract of belladonna  $\frac{1}{12}$  gr.

*Dose.*—1 to 3 pills at bedtime.

[P1-S1] **Asbic Pills** (Lilly, London). Aloin  $\frac{1}{2}$  gr., strychnine  $\frac{1}{80}$  gr., extract of belladonna leaves  $\frac{1}{2}$  gr., ipecacuanha  $\frac{1}{15}$  gr., calomel  $\frac{1}{2}$  gr.

[P1-S1] **Lapactic Pills** (Sharp & Dohme, London). Aloin  $\frac{1}{2}$  gr., strychnine  $\frac{1}{80}$  gr., extract of belladonna  $\frac{1}{2}$  gr., powdered ipecacuanha  $\frac{1}{15}$  gr.

## ALUMINIUM

Al = 26.97.

**Pharmacology.** The soluble salts are gastro-intestinal irritants in large doses but do not cause chronic poisoning. When injected a slow toxic action occurs with fatty degeneration of liver and kidneys.

The use of aluminium cooking vessels is generally considered to be innocuous, although occasional cases of chronic malaise,

possibly due to idiosyncrasy, have been reported, which cleared up on ceasing the use of aluminium utensils.

The physiological action of aluminium compounds is discussed; the action is on the blood system and is observed only when injected. Ordinary amounts have no action by the mouth, and aluminium in the diet in small amounts is harmless. The relief of pain attending the discontinuance of aluminium cooking vessels is due to psychological forces.—J. H. Burn, *Analyst*, 1932, 428.

There is no convincing evidence that aluminium in the amounts in which it is likely to be consumed as a result of using aluminium utensils has a harmful effect upon the ordinary consumer. It is possible that there may be individuals who are susceptible to even such small doses of aluminium as may be derived from aluminium utensils, but evidence of this is inconclusive.—G. W. Monier-Williams, *Rep. publ. Hlth Med. Subj., Lond.*, No. 78, 1935.

**Uses.** Aluminium, in fine powder, may be used for dusting the skin of the abdominal wall as a protective in cases of intestinal fistulæ. The skin is dried and freed from grease and repeated applications of the powder made until a thick film adheres. Alternatively, a paste, known in America as "Baltimore Paste," made by mixing powdered aluminium with sufficient liquid paraffin to produce a stiff paste 1 part and zinc oxide ointment 4 parts, may be employed. This paste is useful for application to the skin round an ileostomy to prevent irritation.

**Alumen** (B.P., U.S.P. XI, *Supp.* II). *Syn.* ALUMEN PURIFICATUM, PURIFIED ALUM.

*Dose.*—5 to 10 grains (0.3 to 0.6 g.).

May be either potassium aluminium sulphate (potash alum),  $KAl(SO_4)_2 \cdot 12H_2O = 474.4$ , or ammonium aluminium sulphate (ammonia alum),  $NH_4Al(SO_4)_2 \cdot 12H_2O = 453.3$ . *Fr. Cx.*, *P. Jap. V*, *P. Helv. V* and *P. Dan.* have potash alum only. In colourless crystals or white powder with sweetish astringent taste.

**Soluble** 1 in 10 of water (potash alum), 1 in 8 (ammonia alum), and 1 in 3 of glycerin; insoluble in alcohol.

**Incompatible** with mercury salts and borax.

**Uses.** As an astringent for local application, solutions of  $\frac{1}{2}$  to 1% or stronger may be used in stomatitis, pharyngitis, leucorrhœa, gonorrhœa, hyperhidrosis and weeping eczema. The solution may be used as a hæmostatic, for example, after tooth extraction, and for superficial abrasions and cuts. Stronger solutions harden the epidermis and are useful in treating soft corns. Ulcers on the lips may be cured by touching with a crystal of alum. As a mouth-wash its solution is possibly not desirable, since destruction of the teeth may occur unless it be quickly removed by rinsing. Internally alum is astringent in small doses and emetic in larger doses such as  $\frac{1}{2}$  to 1 teaspoonful. It is a valuable antidote in acute lead poisoning since it is not only emetic but forms an insoluble sulphate.

**Aqua Hæmostatica** (*P. Ital. V*, *P. Belg. IV*). *Syn.* ACQUA DEL PAGLIARI.

Alum (potash) 80, tincture of benzoin 10, benzoic acid 2, water to 1000. Filtered after allowing to deposit, Pollacci's modification contains 10% of sodium chloride.

**Collyrium Aluminis** (B.P.C.). 1% w/v.

**Gargarisma Aluminis (B.P.C.).** Glycerin of alum, 1 in 8, with acid infusion of roses.

**Glycerinum Aluminis (B.P.).**

Potash alum, 13% *w/w* in water and glycerin. An astringent in chronic pharyngitis; is less disagreeable than tannic acid.

**Injectio Aluminis (L.H.)** for vaginal use. 60 grains in 1 pint.

**Injectio Aluminis et Zinci (St. T. H.).**

Alum 2 parts, zinc sulphate 1 part. Powder and mix.

One or two teaspoonfuls dissolved in 1 pint of warm water for vaginal injection.

**Pessus Aluminis (B.P.C.)** contains 5 gr. (0.3 g.).

**Points of Alum** mounted in wooden cases are prepared for ophthalmic and other uses.

**Pulvis pro Pedibus (P. Helv. V).**

Potash alum 15, talc 85, in fine powder. For tender feet. Another useful form of foot powder is: talc 2, boric acid 2, orris 1, zinc oleate 1.

**Solvellæ Aluminis (B.P.C.)** contain 10 gr. (0.6 g.).

**Alumen Chromicum (B.P.C.).**  $\text{KCr}(\text{SO}_4)_2 \cdot 12\text{H}_2\text{O} = 499.4$ .

Large violet crystals giving a violet aqueous solution which becomes green on heating to  $60^\circ$  to  $80^\circ$ , returning to the original colour on prolonged standing.

**Soluble** 1 in 7 of water; insoluble in alcohol 90%. Used commercially in tanning and as a mordant, also for hardening gelatin in photographic materials.

**Alumen Exsiccatum (B.P.C., P. Helv. V, U.S.P. XI).** *Syn.* ALUM USTUM (*P. Jap. V*), BURNT ALUM. Made by heating potash alum until it has lost 45 to 46% of its weight. *U.S.P. XI* makes from potash or ammonia alum.

**Soluble** slowly and completely 1 in 20 of water. If dried above  $200^\circ$  the product will not dissolve completely owing to formation of oxysulphate.

Is a powerful astringent useful as a dressing for old ulcers and sores. Also used for preserving skins, and as a water-softener.

**Alumen Ferricum (B.P.C.).** *Syn.* IRON ALUM, FERRIC AMMONIUM SULPHATE.  $\text{NH}_4\text{Fe}(\text{SO}_4)_2 \cdot 12\text{H}_2\text{O} = 482.2$ .

*Dose.*—5 to 10 grains (0.3 to 0.6 g.). Amethyst coloured efflorescent crystals, of astringent taste. **Soluble** 1 in 3 of water (best with a little sulphuric acid added), insoluble in alcohol. Internally to arrest hæmorrhage, also as an astringent gargle (2%), throat spray or pigment (8%).

**Aluminii Acetas.**  $\text{Al}_2(\text{C}_2\text{H}_3\text{O}_2)_3$ .

A gummy mass soluble in water, obtained by interaction of lead acetate and aluminium sulphate.

**Aluminii Subacetat.**  $\text{Al}_2\text{O}_3 \cdot 4\text{C}_2\text{H}_3\text{O}_2 \cdot 4\text{H}_2\text{O}$ . *P. Dan.* gives the formula  $\text{Al}(\text{OH})(\text{CH}_3\text{COO})_2$ .

A white powder sparingly soluble in water, obtained by heating a solution of the normal acetate.

Is used as a desiccant and deodorant in powder or with glycerin. For ophthalmia neonatorum a 10% ointment has been used, applied between the lids every hour, in place of silver nitrate drops.

**HÆMORRHAGE, UTERINE AND POST-PARTUM.** 2 to 3% solution of aluminium acetate arrests hæmorrhage from inertia of uterus at child-birth.

**OXYURIASIS.** As an *anthelmintic* aluminium subacetate has been used in treatment of oxyuriasis. *Dose* for an adult 1 g. 3 times daily for three days; for children 0.5 g. twice daily—preceded in each case by a dose of calomel.

**Alumevan (Evans, Sons, Lescher & Webb, Liverpool).** Solution of aluminium acetate (B.P.C.) 1½ fl. oz., syrup 360 m., essence of cherry 4 m., purified honey to 4 fl. oz. *Dose.*—1 drachm 4 times daily after food; a pint of milk should be taken each day. Rheumatoid arthritis and allied bone diseases (*see* communication by A. J. Helfert, *Brit. J. Surg.*, 1940, 27, 651).

**Lenicet Ointment** (*Riddell Products, London*). Polymerised aluminium acetate 5%, anhydrous wool fat 10%, white soft paraffin 85%. In dermatitis, eczema, burns, etc. [P1] **Lenirenin Belladonna Ointment** is composed of Lenicet, adrenine, local anæsthetics and 1% extract of belladonna. For hæmorrhoids, tenesmus, pruritus ani, etc. Also available as suppositories.

**Liquor Aluminiumi Acetas** (*B.P.C., P.G. VI, P. Austr., P. Jap.*). *Syn.* LIQUOR ALUMINII ACETICUS, BUROW'S SOLUTION (Burow's Solution, *P. Belg. IV*, is Liquor Aluminiumi Aceto-Tartratis, similar to *P. Helv. V*). A solution containing a basic aluminium acetate.

Is used on the Continent in place of boric lotion for moist fomentations in cutaneous erysipelas and other dermatoses. Gauze soaked in the solution may be used as a dressing for suppurating wounds. Diluted with twice its volume of water it is used as an antiseptic astringent lotion, and diluted 1 with 4 or more of orange-flower water it forms a pleasant mouth-wash.

A 1 in 8 dilution forms an effective substitute for Calamine Lotion, and in some cases may produce better and quicker therapeutic results.—R. M. B. MacKenna, *Brit. med. J.*, i/1932, 78.

[P1] **Solution de Burow avec Précipité** (*P. Belg. IV*). Potash alum 10, lead acetate 50, water 940. The salts are dissolved in half the water and mixed.

**Liquor Aluminiumi Aceto-Tartratis.** *Syn.* ALUMINIUM ACETO-TARTARICUM SOLUTUM (*P. Helv. V*).

Dissolve aluminium sulphate 30 in warm water 135, cool and add, with stirring, calcium carbonate 13, and then acetic acid (30%) 36, allow to stand 3 days with occasional shaking, filter off the solution and add to every 100 of filtrate tartaric acid  $4\frac{1}{2}$ .

Sp. gr. 1.057 to 1.063. Contains about 10% of aluminium aceto-tartrate. According to *P. Helv. V* this is to be supplied when Burow's solution is ordered.

**Aluminiumi Chloridum** (*B.P.C.*).  $\text{AlCl}_3 \cdot 6\text{H}_2\text{O} = 241.4$ .

*Dose.*—2 to 4 grains (0.12 to 0.25 g.). May be administered in solution or as pills containing 2 gr.

A white, amorphous deliquescent powder. **Soluble** 2 in 1 of water, 1 in 4 of alcohol and in glycerin. Has been found of distinct service in locomotor ataxy; relieves the lightning pains.

**Liquor Aluminiumi Chloridi.** Dissolve aluminium chloride (+6H<sub>2</sub>O) 20, in water to produce 34 by volume = 42.5% by weight. Sp. gr. 1.35.

**Aluminiumi Hydroxidum** (*B.P.C.*).  $\text{Al}(\text{OH})_3 = 78.0$ .

*Dose.*—5 to 10 grains (0.3 to 0.6 g.).

Prepared by pouring hot potash alum solution into a hot solution of sodium carbonate. A white, odourless, tasteless, amorphous powder, **insoluble** in water, soluble in caustic alkali solutions.

**Uses.** For the treatment of flatulence, hyperacidity, pyrosis and allied gastric disturbances. Colloidal aluminium hydroxide is a valuable adjuvant in the treatment of peptic ulcer, the dose advised being 60 to 180 gr. 1 hour after meals.

**PEPTIC ULCER.** The continuous administration of colloidal aluminium hydroxide has advantages over all other forms of treatment and is of particular value in cases of ulcer with massive hæmorrhage. In a series of 101 such patients only 3 died, a mortality percentage far below that for other forms of therapy. Pain is relieved at once and the ulcer heals in 7 to 10 days. The technique of

administration requires constant and continuous medication both day and night. If given in the usual way, not more than one hour should elapse between doses. A preferable method of administration is by the continuous drip method.—E. Woldman and C. J. Polan, *Amer. J. med. Sci.*, 1939, 198, 155.

It has proved itself a highly effective antacid and offers many advantages over the older remedies in the treatment of peptic ulcer. Although it may be used in conjunction with frequent feedings, these are no longer required to control acidity, and one may safely dispense with them if sufficient hydroxide is given. One drachm 3 times daily is often enough to control symptoms and promote healing in some cases. There is evidence that the drug may inhibit gastric secretions when given over a considerable period.—J. F. McIntosh and C. J. Sutherland, *Canad. med. Ass. J.*, i/1940, 140.

Observations on 30 patients indicated that aluminium hydroxide gel is an effective substance for neutralising the gastric contents; that it is a valuable adjuvant in the treatment of peptic ulcer, and that it is not liable to cause alkalosis. In doses of 1 to 3 drachms its neutralising powers are as great as those of ordinary doses of alkaline powder. Nearly all the patients were completely free from pain while taking this preparation, and diarrhoea (often a troublesome complaint while taking alkalis) was absent in every case except one.—T. Izod Bennett and A. M. Gill, *Lancet*, i/1939, 500.

**ULCERATIVE COLITIS.** Good results reported in 26 patients convalescing from acute attacks of ulcerative colitis, from the rectal injection of a mixture of 6 fl. oz. of a preparation containing 20% of kaolin, 10% of liquid paraffin and 70% of an aluminium hydroxide gel, equivalent to  $2\frac{1}{2}\%$  of aluminium hydroxide and 4 fl. oz. of water. Injections were given at first thrice weekly and then gradually reduced to once weekly. The first and second injections were not retained for more than 30 minutes, but retention overnight was possible subsequently. If faeces were being passed three or more times per 24 hours, a small low saline enema was given 2 hours before treatment. Blood streaks in the faeces disappeared in 3 to 4 weeks, sometimes in a much shorter period, the average number of treatments required being 11.4. The treatment must not be used during the acute stages of the disease.—W. Z. Fradkin, *J. Lab. clin. Med.*, 1937, 22, 896.

**Aludrox** (*John Wyeth, London*). A colloidal suspension of hydrated alumina stated to be capable of neutralising in 1 hour the free HCl of 12 vols. of average gastric juice. Its pH is 6.8, so that alkalinity is not produced even with excess. *Dose*.—1 to 2 teaspoonfuls.

**Alocol** (*Wander, London*). Colloidal aluminium hydroxide in powder, or tablets containing 0.5 g. *Dose*.—2 tablets to be dissolved in the mouth  $\frac{1}{2}$  hour before and after each meal.

**Collumina** (*Evans, Sons, Lescher & Webb, Liverpool*). Colloidal aluminium hydroxide for the treatment of gastric inefficiency and abnormal acidity of the stomach.

**Hydronal** (*Bayer Products, London*). Aluminium hydroxide with a strong peptisation action. Supplied in  $7\frac{1}{2}$  gr. tablets.

**Lactalumina** (*Crookes Laboratories, London*). Colloidal aluminium hydroxide. *Dose*.—1 to 2 fluid drachms in water.

**Aluminii Sulphas** (*B.P.C.*). *Syn.* ALUMINIUM TRISULPHATE.  $\text{Al}_2(\text{SO}_4)_3 \cdot 16\text{H}_2\text{O}$  = 630.4. *Fr. Cx.*, *P. Jap.* V, *P. Helv.* V and *P. Dan.* have  $18\text{H}_2\text{O}$ .

*Dose*.—2 to 5 grains (0.12 to 0.3 g.).

White crystalline powder or lumps made by dissolving freshly precipitated aluminium hydroxide in sulphuric acid. *Soluble* 1 in 1 of water nearly; insoluble in alcohol.

*Incompatible* with alkalis and alkaline carbonates.

*Uses.* Similar to alum but more astringent. A saturated solution has been used as a mild caustic for enlarged tonsils and nasal polypi. 5 to 10% solutions may be applied locally to ulcers. A 2% solution may be used for removing wrinkles.



**Kaolinum** (*B.P., Fr. Cx.*). *Syn. and Prop. Names.* BOLUS ALBA (*P.G. VI, P. Jap. V, P. Helv. V, P. Dan.*), BOL BLANC (*P. Belg. IV*), CHINA CLAY, KAYLENE (*Kaylene Ltd., London*). OSMO KAOLIN (*Morson, London; Allen & Hanburys, London*) and COLLOSOL KAOLIN (*Crookes' Laboratories, London*) are brands of colloidal kaolin.

*Dose.*— $\frac{1}{2}$  to 2 ounces (15 to 60 g.), with water or milk. Best on empty stomach.

Native white, hydrated aluminium silicate, purified by elutriation from sandy matter. It is a soft whitish powder.

Although the usual material sold as Kaolin *B.P.* conforms to official standards it is still grossly contaminated with sharp grits undesirable in a medicine designed for internal use. Many of the failures of indiscriminate kaolin therapy can be explained as due to the use of unsuitable preparations, *i.e.*, those containing abrasive gritty contaminants and those which tend to coalesce into sticky masses because they contain uncompensated electrolytes. The therapeutic efficiency of kaolins and allied substances should not be assayed in terms of methylene blue, congo red, or any other dye, but in terms of some definite food poison or decomposition product.—N. Mutch, *Brit. med. J.*, i/1937, 596.

**Insoluble** in all ordinary solvents and in mineral acids.

*Uses.* Kaolin acts as a protective of the mucosa of the stomach and intestines, and may be given as a substitute for bismuth carbonate in gastric and intestinal affections. It does not constipate like bismuth and is superior in that it is unaffected by the gastric juice. It also adsorbs toxins from the alimentary canal, and is valuable in cholera, dysentery, bacillary diarrhoea, food poisoning and in diarrhoea of phthisis. Externally kaolin is a useful absorbent for irritation of the skin. It is a useful filtering medium for clarifying liquids.

**ASIATIC CHOLERA.** A suspension of 800 g. of kaolin in a litre of water may be employed, 3 ounces being given every half-hour until vomiting and diarrhoea abate, then continued every hour and then every two hours up to 12 or 15 hours.

**BURNS.** Spread a thick layer of kaolin powder daily on the burn; cover with gauze and a thin layer of zinc ointment.

**FISTULÆ.** For protection of skin round gastric or intestinal fistulæ opening through the abdominal wall, kaolin is better than ointments.

**Cataplasma Kaolini** (*B.P.*). *Syn.* KAOLIN POULTICE.

Kaolin 52.7%, boric acid 4.5%, with thymol, methyl salicylate, oil of peppermint and glycerin.

Sodium lactate (70%) may be used in place of glycerin in making this preparation.

*Uses.* Kaolin poultice is used as a carrier of heat and moisture in various local inflammations. It has largely replaced the domestic bread and linseed poultices since it retains heat and moisture more efficiently.

**Antiphlogistine** (*Denver Chemical Co., London*—for formula, see Vol. II), **Antithermogen** (*Hewlett, London*), **Caloplast** (*Allen & Hanburys, London*), **Sorbefacin** (*Christy, London*), and **Thermofuge** (*Parke, Davis, London*) are similar preparations used for relieving inflammation.

**Emulsio Paraffini Liquidi et Kaolini** (*B.P.C.*).

*Dose.*— $\frac{1}{2}$  to 2 ounces (15 to 60 ml.).

Contains 25% *v/v* of liquid paraffin and about 80 gr. of kaolin per oz.

**Mist. Kaolin.** (*N.I.F.*). Kaolin 15 gr., sodium bicarbonate 10 gr., heavy magnesium carbonate 10 gr., peppermint water to  $\frac{1}{2}$  oz.

**Pulv. Kaolin. Co.** (*N.I.F.*). *Average dose.*—60 grains.

Sodium bicarbonate 160 gr., heavy magnesium carbonate 320 gr., kaolin 480 gr.

**Unguentum Kaolini** (*B.P.C.*). *Syn.* KAOLIN MASS.

1 in 4 in a paraffin basis. Spread on lint and applied to abraded skin, it allays irritation.

**Carbokaylene** (*Kaylene Ltd., London*). Kaylene colloidal kaolin with activated charcoal. *Dose.*—3 to 4 tablets three times daily half-hour before meals, for flatulence.

**Charkaolin** (*Allen & Hanburys, London*). Colloidal kaolin and activated charcoal in granules and tablets. For intestinal affections.

**Kaldrox** (*John Wyeth, London*). Emulsoid of a 20% colloidal kaolin activated in a 2½% aluminium hydroxide gel. For gastric hyperacidity, intestinal putrefaction and diarrhoea.

**Kaomin** (*Lilly, London*). Powder containing bismuth subcarbonate 100, kaolin 280, magnesium hydroxide 60, sucrose 180, vegetable mucilage 20, vanillin 0.6. For colitis and gastric-intestinal diseases.

**Kaylene-Ol** (*Kaylene Ltd., London*). *Dose.*— $\frac{1}{2}$  ounce before meals. A preparation of kaolin with liquid paraffin for use as an evacuant and adsorbent.

**Lacto-Kaolin** (*Crookes' Laboratories, London*). Combination of Collosoil kaolin and lactose for ulcerative colitis.

**Neutralon** (*Schering, London*). Synthetic aluminium sodium silicate. *Dose.*—A teaspoonful in  $\frac{1}{2}$  glass of water 3 times daily. Astringent, antacid, adsorptive. Gastric hypersecretion, hyperchlorhydria and gastric and duodenal ulcer. [P1] *Belladonna-Neutralon* contains in addition extract of belladonna equivalent to 0.0075% of hyoscyamine; for use where vagal irritability is present.

**Parakaolin** (*Duncan, Flockhart, Edinburgh*). An emulsion of kaolin 20%, with liquid paraffin 33½%, for use in chronic constipation, etc.

**Fuller's earth** is a grey or brown native aluminium silicate containing iron, magnesium and calcium which is dried in kilns over coke fires. It is used largely for decolorising oils, as a filler for various purposes, in cosmetic powders, and for mud baths. A special grade of activated fuller's earth is employed for the recovery by adsorption of vitamin B<sub>1</sub>.

**Cimolite** (*John Taylor, London*) is a special preparation of fuller's earth agreeably perfumed, for toilet and nursery use.

**Terra Alba** in commerce is variously kaolin, gypsum, burnt alum or magnesia, in preference the first.

**Talcum Purificatum** (*B.P.C., U.S.P. XI, Fr. Cx., P. Helv. V*). *Syn.* CRETA GALICA PURIFICATA.

A native hydrated magnesium silicate,  $Mg_3(Si_2O_5)_4(OH)_4$ , purified by treating with boiling dilute hydrochloric acid and washing free from acid. Venetian talc is from the Tyrol.

A soft white powder insoluble in acids and the ordinary solvents. Used in dusting powders to allay irritation and to prevent chafing. Also used as a lubricant for massaging, and in tablet making. Can be used as a filtering medium for clarifying liquids.

**French Chalk** is a harder silicate of magnesium.

**Soapstone.** A hard, massive variety of French chalk, consisting chiefly of magnesium hydrogen silicate,  $Mg_3H_4Si_2O_{11}$ .

**Steatite.** A hydrated magnesium silicate with some aluminium, iron, and lime, used as a furnace lining.

**Bentonite**, mineral soap or soap clay, is a refractory clay of volcanic origin obtained at Fort Benton in the Missouri valley and in California. It consists of the hydrous silicates of aluminium, magnesium and calcium; small amounts of iron are also present. The analysis corresponds to the formula  $(\text{Mg}, \text{Ca})\text{O} \cdot \text{Al}_2\text{O}_3 \cdot 5\text{SiO}_2 \cdot n\text{H}_2\text{O}$ . In contact with water bentonite swells, forming a gelatinous viscous mass and in weak concentration it gives a stable colloidal solution. Gels and colloidal solutions of bentonite are weakly alkaline to litmus and are affected by electrolytes which produce flocculation. The properties of bentonite are unaffected by temperatures up to  $400^\circ$ , thus allowing sterilisation by heat. It does not contain any poisonous principle. Bentonite is recommended for use in pharmaceutical preparations and cosmetics, such as ointments, lotions and emulsions, and formulæ for various preparations are described.—*Pharm. J.*, ii/1939, 528.

**Elkonite**. A naturally occurring colloidal clay found in Nevada. When placed in water it swells to form a firm jelly-like mass. It is much more colloidal than the group of clays known as bentonites, and is essentially an aluminium magnesium silicate. It is moderately detergent and has been used as a soap substitute. In 15% concentration elkonite forms a gel suitable for use as an ointment base, which has advantages over bases in common use in that it dries on the skin, leaving an adherent film which will not rub off or stain clothing, and yet can be readily removed by washing with water.—*M. L. Tainter et al., J. Amer. pharm. Ass., Sci. Edn.*, 1940, 306.

**Magnesium Silicate (Precipitated)**. *Syn. and Prop. Names.* MAGNESIUM TRISILICATE, SYNTHETIC SEPIOLITE, GASTOMAG (*Boots, Nottingham*), MAGSORBENT (*Kaylene Ltd., London*), NOVASORB (*Evans, Sons, Lescher & Webb, Liverpool*).

*Dose*.—5 to 30 grains (0.3 to 2 g.).

A white amorphous magnesium silicate prepared by precipitation on mixing solutions of magnesium sulphate and sodium silicate. The composition of the precipitate varies considerably when made with different proportions of sodium silicate and magnesium sulphate, and good results are said to be obtained with quantities equivalent to the ratio  $2\text{MgO} : 3\text{SiO}_2$ , using sufficient sodium hydroxide with the silicate so as to complete the decomposition of the sulphate.

(For a detailed account of its preparation and composition see Norman Glass, *Quart. J. Pharm.*, 1936, 445.)

Medicinal magnesium trisilicate is defined as a "compound represented by the formula  $\text{H}_4\text{Mg}_3\text{Si}_3\text{O}_{10}$  and giving the pure diffraction radiograph as the natural mineral sepiolite No. 1." The ratio  $\text{MgO} : \text{SiO}_2 = 1 : 2.24$  (gravimetric). Many marketed brands fall entirely to conform with these basal requirements. It is shown that (a) artificial sepiolite No. 1 does not cause alkalosis; (b) the extent and speed of interaction with acids diminish rapidly at hypochlorhydric strengths (within certain limits of dosage the neutralising effect is automatically adjusted to the demands of the gastric juice); (c) within a certain range a useful amount of the silicate can be given in hypochlorhydric states without its neutralising the gastric contents to such an extent as to destroy peptic activity.—*N. Mutch, Brit. med. J.*, ii/1937, 735; see also N. Glass, *ibid.*, 878.

**Insoluble** in water. Interacts slowly with dilute mineral acids with formation of the magnesium salt of the acid and separation of colloidal silica.

**Uses**. Antacid and adsorbent. May prove preferable to other antacids and kaolin, especially in the treatment of peptic ulcer because of its greater adsorptive properties and the moderately slow and even rate of neutralising acid.

Synthetic hydrated trisilicate of magnesium exhibits powerful adsorbent qualities. At the saturation point for methylene blue it is seventeen times as active as colloidal kaolin (room temperature), and at body temperature the disparity is

even greater. Its immediate adsorptive activity is considerable, but several days are required for saturation. The range of its adsorptive affinities covers a great variety of substances, including acid and basic dyes, alkaloids, bacterial toxins, putrefactive amines, and food poisons.—N. Mutch, *Brit. med. J.*, i/1936, 148.

**PEPTIC ULCER.** 15 cases successfully treated by administration of hydrated magnesium trisilicate in doses ranging from 7 to 28 grains (or 5 to 21 grains of the anhydrous substance) mid-way between each feed (feeds at first 2-hourly and later 3-hourly when pain was under control and occult blood tests negative), with 1 to 4 teaspoonfuls of an emulsion of paraffin in a watery dispersion of colloidal kaolin half an hour before each feed. The special features of the employment of a synthetic hydrated magnesium trisilicate are: (1) the combination of antacid, antiseptic and antitoxic actions; (2) a sustained action whereby hydrochloric acid, destructive ferments and toxins can be removed continuously for several hours after administration of a single dose; (3) the possibility of a local therapy at the ulcer base; (4) freedom from the risk of inducing toxic alkalosis.—N. Mutch, *Brit. med. J.*, i/1936, 256.

Magnesium trisilicate in 60 to 120 gr. doses has been fully proved to be an efficient antacid and has no disadvantages except that it often produces constipated motions which irritate the rectum and cause frequent straining at stool.—A. H. Douthwaite, *Practitioner*, ii/1939, 46.

Six-ounce feeds of milk given every two hours with a drachm of aluminium hydroxide or magnesium trisilicate half an hour after each feed will produce complete control of free acidity in almost every case.—*Lancet*, i/1940, 973.

**Magnesil** (*Duncan, Flockhart, Edinburgh*). An antacid mixture containing 60 gr. of synthetic magnesium trisilicate in each fl. oz.

*Dose.*— $\frac{1}{2}$  to 2 tablespoonfuls in water between meals.

[P1] **Magsorbent Atropine Tablets** (*Kaylene Ltd., London*). These contain  $\frac{1}{100}$  gr. of atropine in each, absorbed so that it cannot be removed by the addition of water, but is released in the digestive tract.

**Trinesil** (*Abbott Laboratories, London*). Magnesium trisilicate, tablets 7 $\frac{1}{2}$  gr.

**Diatomite** (*B.P.C.*). *Syn.* PURIFIED SILICEOUS EARTH, PURIFIED KIESELGUHR, TERRA SILICEA PURIFICATA (*U.S.P. XI, P. Dan.*).

Obtained from the siliceous skeletal remains of Diatomaceæ, large deposits being found in Scotland, Germany and elsewhere. The crude material is crushed, ignited, boiled with hydrochloric acid, washed and dried. Occurs as a bulky, white or pale buff odourless powder, *soluble* in alkalis, insoluble in acids except hydrofluoric. Used as an adsorbent dusting powder and as a filtering medium.

**Sodium Silicate.** *Syn.* SOLUBLE GLASS, WATER GLASS.

Is made by fusing silica, fine sand, or powdered flint, powdered coal and dried sodium carbonate mixed in powder, in an earthenware crucible, and pouring out the fused mass on to a stone slab to cool. This is pulverised and treated with boiling water to dissolve the soluble part. The solution is filtered and concentrated. Commercial solutions usually contain about 20% of silica and 10% of soda.

Senile pruritus and other senile skin disorders have been treated by intravenous injections of 1% sodium silicate, each injection representing 0.01 to 0.02 g. of the pure silicate. From 8 to 12 injections necessary, given at intervals of 2 or 3 days. Arteriosclerosis, pulmonary tuberculosis, and stenosis of the cardiac valves are also alleged to have benefited from such injections.

**Silantox** (*Silica Gel, London; Savory & Moore, London*). Colloidal silica. Used internally as an intestinal absorbent and externally as a dusting powder.

## AMMONIUM

[P2] "*Ammonia.*"

[B3] "*Ammonia—in substances not being solutions of ammonia or preparations containing solutions of ammonia; substances containing less than 5%, weight in weight, of ammonia (NH<sub>3</sub>); refrigerators; smelling bottles.*"

**Ammonii Carbonas** (*B.P., U.S.P. XI, Fr. Cx., P. Jap. V, P. Helv. V*).

**Dose.**—5 to 10 grains (0.3 to 0.6 g.). *U.S.P. XI* average dose 5 grains.

White masses with ammoniacal odour and alkaline taste, consisting of a variable mixture of ammonium bicarbonate ( $\text{NH}_4\text{HCO}_3 = 79.05$ ) and ammonium carbamate ( $\text{NH}_4\text{NH}_2\text{CO}_2 = 78.06$ ). It contains 30 to 32.5%  $\text{NH}_3$ .

**Soluble** 1 in 4 of water, 1 in 5 of glycerin. The carbamate portion is soluble in alcohol 90%.

**Incompatible** with acids, iron salts and salts of alkaline earths.

For dispensing, powdered ammonium carbonate is unsuitable since if the bottle is frequently opened ammonium bicarbonate is formed. A 1 in 8 solution has been found to be stable. It is best prepared by suspending translucent lumps, free from powder, in a muslin bag just below the surface of the water in a covered vessel.

**Uses.** Ammonium carbonate is stimulant, carminative and expectorant. Is excreted as urea and has a slight diuretic action. Does not increase alkalinity of blood or urine. Used as a stimulating expectorant in chronic bronchitis, broncho-pneumonia, especially of children, and in cardiac asthma. The solution is a useful application to insect bites and wasps' stings.

**WOUNDS.** Gauze pads soaked with a 2% solution of ammonium carbonate or bicarbonate promote healing in purulent and indolent wounds.—*W. Robinson, Amer. J. Surg.*, 1940, 47, 111.

**Mist. Tuss. (N.I.F.).** Ammonium chloride 5 gr., ammonium carbonate 3 gr., liquid extract of ipecacuanha  $\frac{1}{2}$  m., solution of bordeaux B  $2\frac{1}{2}$  m., chloroform water to  $\frac{1}{2}$  oz.

[P1] **Mist. Tuss. Sed. (N.I.F.).** Potassium bromide 10 gr., ammonium carbonate 3 gr., camphorated tincture of opium  $7\frac{1}{2}$  m., liquid extract of ipecacuanha  $\frac{1}{2}$  m., liquid extract of liquorice 20 m., water to  $\frac{1}{2}$  oz.

### **Liquor Ammoniae Aromaticus (B.P.C.).**

**Dose.**— $\frac{1}{4}$  to 1 drachm (1 to 4 ml.).

Is prepared with ammonium carbonate, strong solution of ammonia and terpeneless oils of lemon and nutmeg and is of the same ammoniacal strength as the official spirit.

It gives a clear mixture with distilled water as distinct from the *B.P.* spirit. It is not so pungent to the taste.

### **Mistura Ammoniae cum Senega (B.P.C.).**

**Dose.**— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.).

Contains 4 gr. of ammonium carbonate and 5 gr. of ammonium chloride with tincture of ipecacuanha, syrup of tolu, and infusion of senega to 1 oz.

### **Spiritus Ammoniae Aromaticus (B.P.). Syn. SPIRIT OF SAL VOLATILE.**

**Dose.**—15 to 60 minims (1 to 4 ml.).

Ammonium carbonate dissolved in a mixture of strong solution of ammonia with a distillate of oil of lemon, oil of nutmeg, alcohol and water. Contains 2.1 to 2.4% *w/v* of  $\text{NH}_3$ .

### **Spiritus Ammoniae Aromaticus (U.S.P. XI).**

**Average dose.**—30 minims (2 ml.).

Prepared by dissolving oils of lemon, lavender and nutmeg in alcohol, adding a solution of ammonium carbonate, and ammonia water, and filtering after 24 hours. It contains more ammonium carbonate and less ammonia than the corresponding preparation of the *B.P.*

**Ammonii Bicarbonas** (B.P.).  $\text{NH}_4\text{HCO}_3 = 79.06$ .

*Dose*.—5 to 10 grains (0.3 to 0.6 g.).

A white crystalline powder or white crystals volatilising slowly at room temperature. **Soluble** 1 in  $5\frac{1}{2}$  of water; insoluble in alcohol 90%.

Is formed from ammonium carbamate when ordinary ammonium carbonate is exposed to air, and has been suggested as a more stable compound for use instead of the carbonate, especially for preparing tablets and capsules.

[P2] **Liquor Ammoniae Fortis** (B.P.).

*Dose*.—3 to 6 minims (0.2 to 0.4 ml.).

Contains 32.5% w/w  $\text{NH}_3$ ; sp. gr. 0.885 to 0.891 ("0.880 ammonia" contains 34.5% w/w  $\text{NH}_3$ ). **AQUA AMMONIAE FORTIOR** (U.S.P. XI) contains 27 to 29%. **AMMONIAQUE OFFICINALE** (Fr. Cx.) 20-18%. **AMMONIACA LIQUIDA** (P. Ital. V, F.E. VIII) is 20%; sp. gr. 0.925.

**Incompatible** with iodine, hypochlorites, salts of heavy metals, notably mercuric chloride and silver salts, and vegetable tannins.

**Antidotes.** Stomach tube and emetic must *not* be used. Give well diluted vinegar freely, or copious drinks of orange or lemon juice. Keep patient lying down and warm. Demulcent drinks, olive oil. Morphine,  $\frac{1}{4}$  gr., hypodermically for pain. Tracheotomy may be necessary.

**Enema Ammoniae.** Strong solution of ammonia 1, water 160 (1 drachm to the pint).

Has been used in post-operative ileus and intestinal paresis. Its effect is enhanced by a dose of pituitary extract hypodermically given  $\frac{1}{2}$  hour previously.

**Linimentum Ammoniae** (B.P.C.).

Contains 25% v/v of solution of ammonia with oleic acid and liquid paraffin. Does not thicken on standing as is the case with liniments made with vegetable oils. Liniment of ammonia is usually supplied for hartshorn and oil.

[P2] **Liquor Ammoniae Domesticus** (vel **Detergens**), **Household Ammonia**.

Oleic acid 1, alcohol 1, mix and add strong solution of ammonia 7, distilled water 7; shake well. For use diluted as a detergent of the skin. In the bath 1 in 1000 to 2000 softens the water; also for general domestic purposes.

[P2] **Cloudy Ammonia** is made with tap water—for this the gravity of the preparation must not be too light, otherwise the lime salts constituting the "cloud" will settle down. The following is a suitable formula:—Dissolve castile soap 1.3 in water 60, and add strong solution of ammonia 27, lime water 0.6, and water to 100.

**Lotio Olei Amygdalae Ammoniata** (B.P.C.). *Syn.* LOTIO CRINALIS, ERASMUS WILSON'S HAIR LOTION.

Almond oil 1 in 8, strong solution of ammonia 1 in 8, with oil of rosemary, in alcohol 90%, and honey water.

For alopecia areata, strong ammonia solution 1, chloroform 1, olive oil 1, spirit of rosemary to 8, is useful.

[P2] **Liquor Ammoniae Dilutus** (B.P.). *Syn.* LIQUOR AMMONIAE, AQUA AMMONIAE (U.S.P. XI, P. Jap. V), AMMONIA LIQUIDA (P. Ned. V), AMMONIUM HYDRICUM SOLUTUM (P. Helv. V).

Contains 10% w/w of  $\text{NH}_3$ . [P2] **AMMONIAQUE OFFICINALE DILUË** (Fr. Cx.) is about the same strength. Exposure to the fumes may cause injury to the eyes.

*Dose.*—10 to 20 minims (0.6 to 1.2 ml.).

*Hypodermically* 2 to 6 minims for collapse; or up to 36 minims for snake poisoning.

Internally it is stimulant, diuretic and diaphoretic. Used as a restorative by inhalation, it acts by reflex stimulation of heart and respiration. In embolism large doses of ammonia, well diluted, tend to reduce the coagulability of the blood.

**Ammonii Acetas** (B.P.C.).  $\text{CH}_3\cdot\text{COONH}_4 = 77.08$ .

*Dose.*—10 to 30 grains (0.6 to 2 g.).

This salt is obtainable in white crystals, very soluble in water.

Incompatible with mineral acids, alkaline carbonates, potassium chlorate and dichromate, and with mercurous nitrate.

Serviceable in all fevers and in delirium tremens, one drachm every hour at first, reduced gradually.

### **Liquor Ammonii Acetatis Fortis** (B.P.).

*Dose.*—15 to 60 minims (1 to 4 ml.).

Prepared by neutralising glacial acetic acid with ammonium carbonate and a sufficient quantity of strong solution of ammonia, and diluting the product with distilled water. It contains 57.5% w/v of  $\text{C}_2\text{H}_7\text{O}_2\text{N}$  and has a pH of 7.0 to 8.0.

**Liquor Ammonii Acetatis Dilutus** (B.P.). *Syn.* LIQUOR AMMONII ACETATIS, SOLUTION OF AMMONIUM ACETATE, SPIRIT OF MINDERERUS.

*Dose.*— $\frac{1}{4}$  to 1 ounce (8 to 30 ml.).

Strong solution of ammonium acetate 1 part, distilled water to 8 parts. It contains 7.2% of  $\text{C}_2\text{H}_7\text{O}_2\text{N}$ .

Keep in lead-free stoppered bottles.

**Liquor Ammonii Acetatis** (U.S.P. XI).

*Average dose.*— $\frac{1}{2}$  ounce (15 ml.).

Prepared so as to yield a solution containing free acetic acid and carbon dioxide, and for dispensing purposes it is required to be freshly prepared. It is made by dissolving 5% of solid ammonium carbonate in dilute acetic acid (5.7 to 6.3%) or by mixing a 10% w/v solution of ammonium carbonate with a 32% v/v solution of acetic acid (36 to 37%) in water. *P. Helv. V* and *P. Jap. V* contain 15 to 16% of ammonium acetate. Acetate d'Ammonium Dissous (*Fr. Cx.*) contains 18.6 w/v.

**Liquor Ammoniae Anisatus** (B.P.C.). *Syn.* SPIRITUS AMMONIAE ANISATUS.

*Dose.*— $\frac{1}{4}$  to 1 drachm (1 to 4 ml.).

Contains 16.67% v/v of dilute solution of ammonia with oil of anise in alcohol 90%. Several foreign pharmacopœias, e.g., *P.G. VI*, give similar formulæ.

### **Mistura Ammonii Acetatis Composita** (B.P.C.).

*Syn.* MISTURA DIAPHORETICA.

*Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.).

Potassium citrate 20 gr. with strong solution of ammonium acetate, spirit of nitrous ether and spirit of chloroform in camphor water to 1 oz.

**Mist. Salin.** (N.I.F.). *Syn.* MIST. DIAPHORET.

Potassium citrate 10 gr., strong solution of ammonium acetate 8 m., concentrated solution of ethyl nitrite 2 $\frac{1}{2}$  m. (equivalent to spirit of nitrous ether 20 m.), water to  $\frac{1}{2}$  oz.

[P.] **Mistura Anti-Catarrhalis** (Burney Yeo.).

Solution of ammonium acetate 3 dr., spirit of nitrous ether 1 dr., tincture of opium 10 m., ipecacuanha wine 5 m., camphor water to 1 $\frac{1}{2}$  oz. To be taken at night. Assists action of skin and kidneys.

**Ammonii Citras** (*B.P.C.*).  $C_3H_4 \cdot OH(COONH_4)_3, H_2O = 261.2$ .

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 g.).

A deliquescent white powder tending to lose ammonia to form an acid salt. Very *soluble* in water.

A mild expectorant and diuretic acting similarly to the acetate.

**Liquor Ammonii Citratis Dilutus** (*B.P.C.*). *Syn.* LIQUOR AMMONII CITRATIS.

*Dose.*—2 to 6 drachms (8 to 24 ml.).

Contains about 15% w/v of ammonium citrate. Store in green bottles.

**Liquor Ammonii Citratis Fortis** (*B.P.C.*).

*Dose.*— $\frac{1}{2}$  to 1 $\frac{1}{2}$  drachms (2 to 6 ml.).

Four times as strong as the above.

**Ammonii Nitras**.  $NH_4NO_3$ .

*Dose.*—5 to 20 grains (0.3 to 1.2 g.).

Occurs in colourless crystals, m.p. 165°. 7 $\frac{1}{2}$  gr. tablets, enteric coated, have been administered in conjunction with the ketogenic diet (*see Vol. II*) to render the urine acid in the treatment of chronic bacilluria. The fused salt is used for making nitrous oxide.

Doses of 10 to 12 grains daily frequently maintain diuresis and diminish œdema in cardiac insufficiency, where other drugs fail. Disguise taste with syrup of orange.—P. Vallery-Radot and E. Gilbrin, *Brit. med. J. Epit.*, ii/1932, 18.

## AMPULLÆ

### Ampoules

Ampoules are hermetically sealed containers, commonly made of glass, and intended usually for preparations to be used for parenteral administration. Thin glass ampoules covered with cloth are also used for substances such as amyl nitrite for purposes of inhalation, the ampoule being crushed in the fingers and the vapour of the liquid inhaled.

Since ampoules hold sufficient material for one dose only, thus avoiding the risk of infection during the withdrawal of successive doses suffered by multiple-dose containers, and since also there is no possibility of the contents losing their sterility during storage, they present by far the best means of dispensing sterile preparations. They vary in shape, and their capacities range from 0.5 ml. (8 minims) to 100 ml. (3 $\frac{1}{2}$  fl. oz.). Ampoules should be made of good quality, alkali-free glass, and when required for solutions of certain substances such as alkaloidal salts, adrenaline, extract of pituitary, insulin, etc., they must conform with the tests for the limit of alkalinity described in the *B.P.* The tests are on whole and crushed ampoules. The test on the whole ampoules requires the ampoules, up to a capacity of 25 ml., to be filled with a standard\* acid solution of methyl red, sealed and heated. They comply with the test if the colour of the solution has not changed from pink to a full yellow. For the second test the ampoules are crushed and sieved. The particles which pass through a No. 25 sieve, but fail to pass through a No. 36, are washed with alcohol, dried and boiled for half an hour with the test solution, the colour of which must not change from pink to a full yellow. Both tests would



appear to need modification. The former, which requires each ampoule to be filled to its prescribed capacity, is much more severe on a 1 ml. ampoule for example than on a 2.5 ml. ampoule, whilst the latter prevents the use of ampoules which have been coated on their inner surface with a film of resistant glass to enable them to pass the test on whole ampoules. The use of ampoules of coloured glass for preparations unstable to light is of doubtful value. It is preferable to ensure that they are kept in their boxes in order to minimise the effect of light.

Ampoules as received from the manufacturers are usually sealed. Before use they are unsealed, thoroughly washed with distilled water, and sterilised either in an autoclave at 115° for 30 minutes or in a hot air oven at 150° for one hour. Great care should be taken to guard against fragments of glass remaining in the ampoules, since autoclaving causes some batches of glass to flake. They should be examined by shaking well in a good light.

Since ampoules are single dose containers, solutions contained in them do not need the addition of a bacteriostatic, equivalent to 0.5% of phenol, providing they are sterilised by an *absolute* method such as autoclaving. Where the emergency process of the B.P. is applied, the phenol may only be omitted if the preparation is intended for intravenous injection.

Ampoules may be filled on a small scale by means of a hypodermic syringe, and on a large scale by means of a burette fitted with a hypodermic needle, or by inverting the empty ampoules in the solution, placing under reduced pressure and then releasing the pressure, when the solution will be sucked into the ampoules. Ampoules should always be filled with more than the required dose to facilitate withdrawal with the syringe of the required volume, e.g., 1.1 ml. should be put in for a dose of 1 ml.

Sealing is done in the blow-pipe flame and it should be tested by placing the ampoules in some coloured solution, and then warming and cooling the latter, or by placing the ampoules immersed in the solution under reduced pressure and releasing the pressure. The coloured solution will enter any ampoules which are improperly sealed and these should be rejected.

*Each ampoule should be individually labelled with the name and strength of its contents, such as 1 ml. = 0.02 g. Morph. Hydrochl.*

Ampoules may also be used as containers for solid substances, such as neoparsphenamine, sodium citrate, sodium bicarbonate or iodophthalein required for the preparation of sterile solutions. Such solutions are made by adding sterilised water to the solid in the ampoule, dissolving, and using immediately. Special aseptic precautions must be taken with the preparation of these as it is rarely possible to heat and sterilise the final sealed container.

Solutions in ampoules for injection are issued under proprietary names, such as **Ampulique** (Hewlett, London), **Azoule** (Allen & Hanburys, London), **Glaseptic** (Parke, Davis, London), **Hypoloid** (Burroughs Wellcome, London), **G.L.** (Glaxo Laboratories, London), **Sterules** (Martindale, London), **Tubunic Ampoule Syringe** (Roche Products, Welwyn Garden City), consisting of a collapsible tube filled with the solution and fitted with a needle.

## AMYGDALA AMARA

*B.P.C., U.S.P. XI, Fr. Cx., P. Helv. V.*

The dried ripe seeds of *Prunus communis* var. *amara*. Contains 50% of fixed oil and 3 to 4% of amygdalin, and yields 3 to 4% of essential oil.

**Antidotes.** Treat as for poisoning by hydrocyanic acid, see p. 71.

[P1] **Aqua Amygdalæ Amaræ** (I.A.) contains 0.1% of HCN.

*Average dose.*—1 drachm.

**Lotio Amygdalæ Amaræ** (B.P.C.). *Syn.* MISTURA AMYGDALÆ AMARÆ.

Bitter almond 7½% w/v in water.

**Oleum Amygdalæ** (B.P., *P. Helv. V, P. Dan.*) is expressed from the seeds of the bitter or the sweet almond. The content of oil in bitter almonds is about 50% and in sweet almonds about 45 to 50%. The residue from bitter almonds is utilised for the production of essential oil of bitter almond.

**Soluble** in all proportions in chloroform, about 1 in 2½ of ether and slightly in alcohol 90%.

[P1-S1] **Oleum Amygdalæ Amaræ** (B.P.C., U.S.P. XI).

*Syn.* OLEUM AMYGDALÆ ESSENTIALE.

*Dose.*—¼ to 1 minim (0.016 to 0.06 ml.).

The natural oil may contain up to 10% of HCN but is adjusted to contain from 2 to 4%. It is stated that the presence of the HCN retards oxidation of the benzaldehyde to benzoic acid. The oil can also be distilled from apricot and peach kernels.

**Oleum Amygdalæ Volatile Purificatum** (B.P. *Add. II*).  
*Syn.* OLEUM AMYGDALÆ AMARÆ SINE ACIDO HYDROCYANICO (B.P.C.), OLEUM AMYGDALÆ AMARÆ (S.A.P.).

*Dose.*—¼ to 1 minim (0.016 to 0.06 ml.).

Consists of the above essential oil freed from HCN by treatment with ferrous sulphate and calcium hydroxide, and redistillation. Contains not less than 95% w/w of benzaldehyde.

**Spiritus Amygdalæ Amaræ** (B.P.C.). *Syn.* ESSENCE OF BITTER ALMONDS. 1 in 16.

**Benzaldehydum** (B.P.C.).  $C_6H_5 \cdot CHO = 106.0$ .

*Dose.*—¼ m. (0.03 ml.).

A colourless or slightly yellow liquid, sp. gr. about 1.051, solidifying at about 26° and boiling at about 180°. Used as a flavouring agent in place of the natural oil of bitter almond.

**Amygdala Dulcis** (B.P.C.). *Syn.* SEMEN AMYGDALI DULCIS (*Fr. Cx., P. Jap. V*).

The dried ripe seeds of *Prunus communis* var. *dulcis*. Contains fixed oil but no amygdalin.

**Lotio Rosæ** (B.P.C.). *Syn.* MILK OF ROSES. A perfumed emulsion of sweet almond, 1 in 10, with white beeswax and almond oil.

**Mistura Amygdalæ** (B.P.C.).

*Dose.*—¼ to 1 ounce (15 to 30 ml.).

Compound powder of almond 1 in 8 in water. A demulcent vehicle for cough mixtures and for suspending liquids not miscible with water.

**Pulvis Amygdalæ Compositus** (B.P.C.). A mixture of powdered sweet almond, sucrose and acacia.

**Oleum Persicæ** (B.P.C.). *Syn.* PEACH OR APRICOT KERNEL OIL (or mixtures). Is obtained from the kernels of *Prunus Persica* (peach) or *Prunus Armeniaca* (apricot). The latter is used almost exclusively. The oil is used instead of almond oil in the culinary arts and for face creams, etc.

[Pl] **Aqua Armeniacæ** (P. Jap. V). Apricot water, containing 0.1% of HCN.

## AMYLUM

B.P., U.S.P. XI, Fr. Cx., P. Dan., P. Helv. V, P. Jap. V, etc.

Maize starch, from *Zea Mays*, is the only variety official in B.P. '32 and U.S.P. XI, but B.P. Add. I admits also rice starch (*Oryza sativa*). The Committee on Pharmacy and Pharmacognosy of the Pharmacopœia Commission (Report 13) have recommended the addition to the B.P. monograph of wheat (*Triticum aestivum*) and potato (*Solanum tuberosum*) starches. Other pharmacopœias include arrowroot starch from *Maranta arundinacea*. Potato starch, by treatment with hydrochloric acid, yields **Amylum Solubile**. Soluble starch is readily soluble in hot water.

**Cataplasma Amyli** (B.P.C.). Starch 10% boiled with water.

**Cataplasma Amyli** (St. J. H.).

Boric acid 1 dr., starch 1 oz., cold water 2 oz., boiling water to 20 oz.

One of the very safest remedies to apply to an inflamed, weeping or crusted surface and many cases of infantile eczema can be completely cured by its continued use alone.—J. E. M. Wigley, *Practitioner*, 1935, 353.

**Glycerinum Amyli** (B.P.).

Starch 8.5% w/w heated with water and glycerin at not over 140° until it gelatinises. Wheat starch is stated to be most suitable for producing a stable preparation.

**Glyceritum Amyli** (U.S.P. XI).

Starch (maize) 1, water 2, glycerin 7, heated to 140° to 144°.

**Glyceritum Amyli** (Fr. Cx.). Wheat starch 1, water 1, glycerin 13. This is used as the base for a number of glycerita in Fr. Cx.

**Mucilago Amyli**. Heat 16 oz. of water to boiling, add  $\frac{1}{2}$  oz. of starch previously rubbed down with 4 oz. of water, and again raise to boiling.

**Maranta** (B.P.C.). *Syn.* ARROWROOT. The starch from *M. arundinacea* (Marantaceæ). 1 tablespoonful to the pint of hot water produces a demulcent mucilage.

**Mucilago Marantæ**.

Triturate arrowroot 6 dr. with water 2 oz. to make a smooth paste and make up with boiling water to 1 pint. Heat until semi-transparent. Cool and add spirit of chloroform 2 dr.

To suspend heavy medicaments this and a similar preparation of cornflour have been found useful. It will suspend bismuth salts in a proportion as high as 1 drachm to the ounce.

**Lycopodium** (B.P.C., P. Helv. V, U.S.P. XI, Fr. Cx.). The spores of the clubmoss, *Lycopodium clavatum* (Lycopodiaceæ). U.S.P. XI requires not more than 0.75% of acid-insoluble ash. As a pill powder, also as a diluent for insufflations for the throat,

nose, and ear, and as a dusting powder. Its use in quantitative microscopy is based on the presence of 94,000 spores per mg.

**Tinctura Lycopodii** (B.P.C.).

*Dose*.— $\frac{1}{4}$  to 1 drachm (1 to 4 g.). 1 in 10.

To stop frequent micturition and irritation of the bladder.

## ANETHUM

(with ANISUM, ANTHEMIS, etc.)

**Anethum** (B.P.). *Syn.* DILL.

Consists of the dried ripe fruits of *Anethum graveolens* Linn.

**Oleum Anethi** (B.P.).

*Dose*.—1 to 3 minims (0.06 to 0.2 ml.).

Distilled from dill, it is a yellow oil with odour resembling caraway. Sp. gr. 0.900 to 0.915. It contains not less than 43 to 63% w/w of carvone,  $C_{10}H_{14}O$ .

**Soluble** 1 in 1 of alcohol 90% and 1 in 10 of alcohol 80%.

**Aqua Anethi Concentrata** (B.P.) is prepared with 2% v/v of oil of dill, and is approximately 40 times the strength of the distilled water.

**Aqua Anethi Destillata** (B.P.) is prepared by distillation from dill.

**Anisum** (B.P.C., *Fr. Cx.*, *P. Helv. V*). Anise (aniseed) is the dried ripe fruit of *Pimpinella Anisum* (Umbelliferae). Contains  $1\frac{1}{2}$  to  $3\frac{1}{2}$ % of a volatile oil containing anethole.

**Aqua Anisi Concentrata** (B.P.C.).

*Dose*.—5 to 15 minims (0.3 to 1 ml.).

Contains 2% v/v of oil and is approximately 40 times the strength of the distilled water.

**Aqua Anisi Destillata** (B.P.C., U.S.P. XI). Distilled from anise, 1 in 10.

**Syrupus Anisi** (B.P.C.).

*Dose*.— $\frac{1}{4}$  to 1 drachm (2 to 4 ml.).

Concentrated anise water 1, syrup to 8.

**Anisi Stellatum** (B.P.C.). *Syn.* STAR ANISE FRUIT, BADIANE DE CHINE (*Fr. Cx.*). The ripe fruits of *Illicium verum* (Magnoliaceae), containing about 5% of volatile oil.

A fatal case of poisoning in Malaya by *Illicium religiosum* taken in mistake for *I. verum*. The distinctions between the toxic and harmless species are not very marked, but the taste of the seed of *I. religiosum* is pungent and bitter, and the odour resembles oil of cajuput or cardamom.—I. A. Simpson, per *Trop. Dis. Bull.*, 1936, 634.

*I. religiosum* goes by the name of "Badiane" in China and Japan, and in the Philippines a decoction named "sanki" is made from the fruit and is used for its stimulating effects. *I. religiosum*, being cheaper, is often used as a substitute for the non-toxic variety.—Per *Trop. Dis. Bull.*, 1936, 634.

**Japanese Star Anise** (*Illicium religiosum*) is smaller and less regular in appearance, and contains a poisonous principle sikamin. The volatile oil contains saffrole.

**Oleum Anisi** (B.P., U.S.P. XI, *Fr. Cx.*).

*Dose*.—1 to 3 minims (0.06 to 0.2 ml.).

Volatile oil from anise or from star anise, the latter source being used exclusively in this country. Colourless or yellowish oil congealing at not lower than 15° and melting again at not below 17°. Sp. gr. 0.980 to 0.994.

**Elixir Anisi (B.P.C.).** *Dose.*— $\frac{1}{2}$  to 2 drachms (2 to 8 ml.). Contains oils of anise, fennel and bitter almond (without HCN), in alcohol, syrup and water.

**Linctus Anisi (C.X.H.).**  
Oil of anise 1 m., chloroform 1 m., vinegar of squill 10 m., liquid extract of liquorice 10 m., mucilage of tragacanth to 1 dr.

**Spiritus Anisi (B.P.C.).** *Dose.*—5 to 20 minims (0.3 to 1.2 ml.). 1 in 10 in alcohol 90%. U.S.P. XI has the same strength in alcohol 95%.

**Anetholum (B.P.C.).** *Syn.* *p*-METHOXYPROPENYLBENZENE.

$C_9H_{10}(OCH_3)C_2H_5 = 148.1$ .  
*Dose.*— $\frac{1}{2}$  to 3 minims (0.03 to 0.2 ml.).

A white crystalline mass with characteristic anise odour and taste; m.p. 22° to 23°, congealing at 21° to 22°.

**Anthemis (B.P.C.).** *Syn.* ROMAN CHAMOMILE (*Fr. Cx.*), FLOS CHAMOMILLÆ ROMANÆ (*P. Helv. V.*).

The dried double or semi-double flowerheads of cultivated varieties of *Anthemis nobilis* (Compositæ). Tonic, aromatic and stomachic; emetic in large doses. The infusion ("chamomile tea," 1 in 20, *dose* 1 to 4 ounces) is a domestic remedy for indigestion, and a tincture (2 of fresh flowers in alcohol 90% 3 and water 1, *dose* 3 to 10 minims), has been given for summer diarrhoea of children. A decoction with poppy heads is used as a fomentation.

**Extractum Anthemidis (B.P.C.).** *Dose.*—2 to 8 grains (0.12 to 0.5 g.). The soft aqueous extract with added oil of chamomile.

**Extractum Anthemidis Liquidum (B.P.C.).** *Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.). 1 in 1.

**Kamillosan (Camden Chemical Co., London).** A pharmacologically tested and clinically effective preparation of fresh chamomile. Has disinfecting, deodorising and astringent properties. For enemas, fomentations and gargles.

**Oleum Anthemidis (B.P.C.).** *Dose.*— $\frac{1}{2}$  to 3 minims (0.03 to 0.2 ml.).

Distilled from anthemis. A blue liquid when freshly distilled (due to the presence of azulene) becoming greenish and then brownish-yellow. **Soluble** in less than its own vol. of 90% alcohol.

**Matricaria (B.P.C.).** *Syn.* GERMAN CHAMOMILE FLOWERS, FLOS CHAMOMILLÆ (*Fr. Cx.*, *P. Jap. V.*, *P. Helv. V.*, *P. Dan.*).

*Dose.*—2 to 4 drachms (8 to 16 g.).  
The dried flowerheads of *Matricaria Chamomilla*. They have a hollow conical receptacle and no paleæ, while the receptacles of *Anthemis nobilis* are solid and covered with concave, blunt, narrow bracts. Used for the same purposes as anthemis. Oil of German chamomile is inferior in odour to oil of *Anthemis nobilis*.

**Fœniculum (B.P., Fr. Cx., P. Jap. V., P. Helv. V., P. Dan.).**  
*Syn.* FENNEL FRUIT.

*Dose.*—5 to 10 grains (0.3 to 0.6 g.).  
The dried ripe fruits of cultivated plants of *Fœniculum vulgare* (Umbelliferae). Contains volatile oil.

Given to infants in form of Aqua Fœniculi.

**Aqua Fœniculi Concentrata (B.P.C.).**

*Dose.*—5 to 15 minims (0.3 to 1 ml.).  
Contains 2% of oil and is approximately 40 times the strength of the distilled water.

**Aqua Fœniculi Destillata (B.P.C.).** *Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.). Represents 10% of fennel.

**Oleum Fœniculi** (*B.P.C., U.S.P. XI, P. Jap. V.*)

*Dose.*— $\frac{1}{2}$  to 3 minims (0.03 to 0.2 ml.).

Contains anethole, also fenchone,  $C_{10}H_{16}O$ . *Soluble* 1 in 3 to 5 parts of alcohol 90%. Aromatic carminative, usually given as Aqua Fœniculi.

## ANEURINÆ HYDROCHLORIDUM

*B.P. Add. III.*

$C_{12}H_{17}ON_4SCl, HCl, H_2O = 355.2$ .

*Syn.* ANEURINE CHLORIDE HYDROCHLORIDE, VITAMIN  $B_1$ , THIAMINE HYDROCHLORIDE (*U.S.P. XI Supp. II*), THIAMIN CHLORIDE.

*Dose.*—Prophylactic (daily)  $\frac{1}{100}$  to  $\frac{1}{1000}$  grain (0.0003 to 0.0006 g.), equivalent to 100 to 200 units; therapeutic (daily)  $\frac{1}{100}$  to  $\frac{1}{33}$  grain (0.0006 to 0.0018 g.) equivalent to 200 to 600 units. (For further details as to dosage see USES.)

The hydrochloride of 3-(4'-amino-2'-methylpyrimidyl-5'-methyl)-4-methyl-5- $\beta$ -hydroxyethylthiazolium chloride, prepared synthetically or from rice polishings, yeast and other natural sources. It occurs as a colourless, crystalline substance with a faint, yeast-like odour; m.p.  $245^\circ$  to  $250^\circ$  with decomposition.

*Soluble* about 1 in 1 of water; less soluble in glycerin and alcohol; insoluble in oils, ether, acetone and other fat solvents.

Aneurine hydrochloride is present in a number of vegetable food-stuffs, but even in the most abundant sources, namely the germ of cereals and yeast, the amount does not exceed 5 p.p.m. Animals are unable to synthesise or store it in any quantity, and with the exception of liver, milk, eggs and lean pork, foods of animal origin are poor sources of aneurine. The vitamin is stable in the dry form (heating at  $100^\circ$  for 24 hours does not diminish its potency). In aqueous solution it is fairly stable in the presence of weak acids, but is unstable in the presence of alkalis. Solutions may be sterilised by heating in an autoclave at  $120^\circ$  for half an hour if the pH is maintained below 5.5.

Since 1938, the international unit for aneurine hydrochloride has been defined as the antineuritic activity of 3 microgrammes of the international standard preparation of crystalline aneurine hydrochloride. In addition, however, various other units have been defined, due to the number of different methods of assay which have been described. While it is impossible to estimate accurately the equivalence of these units, nevertheless it is possible to make rough approximations, and the following values have been suggested—one international unit equals one Roscoe unit, 2 Chase-Sherman units, and 0.5 Smith-curative unit.

*Incompatibilities.* Mercuric chloride, iodides, carbonates, acetates and ferric sulphate. Tannic acid, iron ammonium citrate and iodine produce brown precipitates. Soluble phenobarbitone produces a white, crystalline precipitate, so that when phenobarbitone is desired in combination with an elixir of thiamine, the base should be used.—L. Greengard, *J. Amer. pharm. Ass., pract. Pharm. Edn.*, 1940, 230.

Pure thiamin hydrochloride will reduce Benedict's solution *in vitro*; this should be borne in mind in the diagnosis of diabetes.—R. S. Hart *et al.*, *J. Amer. med. Ass.*, 1/1939, 423.

**Human Requirements.** Owing to the fact that aneurine is not stored in the body and is rapidly lost from the tissues during short periods of deficiency, normal health cannot be maintained unless the diet regularly contains an adequate amount of the vitamin. At present there is no method available for making an accurate estimation of borderline degrees of aneurine deficiency, but from such information as is available it is possible to arrive at a rough approximation. Cowgill has shown that the minimum aneurine requirements tend to vary greatly not only between individuals but even in the same individual under different physiological conditions, and that they appear to depend on the bodyweight, the calorie requirement, and the carbohydrate intake (the larger the bulk of carbohydrate in the diet, the greater the need for aneurine). These variables are expressed in the formula (*Cowgill's Formula*):  
$$\text{Aneurine requirements} = \text{Bodyweight in Kg.} \times \text{Calorie requirement} \times 0.0000284.$$
  
This worker places the daily requirements for the vitamin at 10 i.u. per 100 calories of food intake.

The Council on Pharmacy and Chemistry of the American Medical Association (1940) consider, in the light of present knowledge, that the minimum daily requirement is not less than 50 i.u. for infants and 200 i.u. for the average adult, though other authorities consider that the average adult intake should be between 300 and 400 i.u. On the basis of present indications it would seem that infants, children and adolescents require a larger daily intake than adults in proportion to the caloric needs, while pregnant and nursing women are said to require from three to five times the normal intake.

While an average well-balanced diet would yield these minimum requirements, it is widely held that the diet of large sections of the poorer classes of the community, containing as it does an unduly high proportion of carbohydrate and white bread, is on or below the borderline of deficiency. This deficiency could be largely overcome by the substitution of wholemeal bread for white bread. There are two difficulties, however, in the way of achieving this, one being that wholemeal flour does not keep so well as white flour, and the other that in spite of persistent propaganda on the part of dietitians the public continues to prefer white bread to wholemeal. In order to overcome these difficulties and to meet the admitted deficiency of aneurine intake, the Government have arranged (1941) for the large-scale production of wholemeal flour and bread and are taking steps for enriching all white flour with aneurine and a calcium compound.

**Physiological Action.** Aneurine is fundamentally associated with carbohydrate metabolism. In combination with pyrophosphoric acid it acts as the co-enzyme of carboxylase, an enzyme essential for the breakdown of pyruvic acid in the body. In the absence of aneurine, pyruvic acid accumulates in the tissues which

in consequence lose their power to take up oxygen. The heart and nervous system are the organs most markedly affected and the severe symptoms of aneurine deficiency occur earliest in these structures.

**Uses.** The most important symptoms of aneurine deficiency are degeneration of the nervous system, cardiac enlargement and dysfunction, œdema, gastro-intestinal disturbances, anorexia, and muscular atrophy. Beri-beri is the most serious clinical result of prolonged aneurine deficiency, the nervous, cardiovascular and alimentary systems all being affected. Acute cases respond rapidly to aneurine therapy, but in chronic cases the treatment is not so successful. Other conditions which are known to be due to marked aneurine deficiency are alcoholic polyneuritis and the polyneuritis of pregnancy; in these instances there is an extremely high carbohydrate and fat intake, or a very low food retention, both of which call for additional aneurine. The oral administration of 5 to 10 mg. for two or three days, with a subsequent reduction of dosage, often leads to a striking improvement. Alternatively, the same doses may be given intramuscularly or even intravenously. Other forms of neuritis which are not definitely known to be due to aneurine deficiency but which nevertheless respond well to treatment, are sciatica, neuralgia, the nerve pains of tabes dorsalis, neuritis due to treatment with metals such as lead and arsenic, and that associated with diabetes. A dosage of 2 to 4 mg. daily is usually sufficient to secure improvement in these cases. Good results have also been obtained in gastro-intestinal disturbances, especially those associated with intestinal atony, constipation and loss of appetite. In these conditions aneurine is best given by intramuscular injection in a dose of 1 or 2 mg. daily. Patients on special diets, such as the routine diets for gastric and duodenal ulcer, or the high carbohydrate diets sometimes employed in nephritis, require a supplementary source of aneurine, and in febrile conditions there is an increase in the aneurine requirement.

There is evidence to suggest frequent deficiency of vitamin B<sub>1</sub> in the human dietary. At the present time only the state of extreme vitamin B<sub>1</sub> deficiency is usually diagnosed. Lesser degrees of B<sub>1</sub> avitaminosis in human beings rarely receive clinical recognition. Experimental results indicate that amounts of B<sub>1</sub> greater than the quantity necessary to protect against extreme deficiency (*i.e.*, beri-beri) produce beneficial effects in lesser deficiencies in both animals and man. Results of a previous study indicate a relationship between vitamin B<sub>1</sub> deficiency and disturbances of the carbohydrate metabolism. In a study of 100 cases of clinical neuritis in which vitamin B<sub>1</sub> was administered orally in a dose of 10 mg. daily, 44 were rendered symptom-free, 48 were improved and 8 showed no benefit. In a group of 8 cases of unexplained gastro-intestinal hypotonicity and anorexia, 6 became free from all symptoms on ingestion of vitamin B<sub>1</sub>; 2 were improved. The use of a single agent—pure vitamin B<sub>1</sub>—is urged in the study and treatment of suspected B<sub>1</sub> avitaminosis.—M. G. Vorhaus, R. P. Williams and R. E. Waterman, *J. Amer. med. Ass.*, ii/1935, 1580.

**BERI-BERI.** The amounts of vitamin B<sub>1</sub> given in the treatment of cardiac beri-beri are often much too small. The therapeutic dose should never be less than four times the maintenance dose which, in the average male, is approximately 1 mg. of the crystalline product. It follows that the therapeutic dose should be at least 5 mg. daily and in some circumstances doses as high as 50 mg. are reasonable.—N. H. Fairley, *Practitioner*, ii/1939, 496.



**ECZEMA.** It is possible in practically all cases to cure eczema by the administration of vitamin B complex. In a few days the itching disappears and healing begins. Generally in a week or ten days the acute eczema and chronic cases are definitely better, though the time required for complete healing varies. When a patient has been cured he may be continuing the treatment, in smaller dosage, prevent relapses.—K. P. Kristensen and S. N. Vendel, *Lancet*, i/1940, 170.

**NEURITIS.** Daily intramuscular injections in alternate arms of 1 mg. (400 pigeon units) of vitamin B<sub>1</sub> gave good results in neuritis. Of 14 resistant cases of neuritis, 8 were cured and 4 were very much improved, and of 18 cases of sciatica 6 were cured and 6 very much improved. In all cases there was a marked degree of improvement in general bodily health. The treatment should be combined with some form of electrotherapy, with or without massage.—D. Stevenson, *Practitioner*, i/1938, 301.

Complete relief of pain in 7 out of 10 patients suffering from peripheral vascular disease was obtained by the intravenous administration of vitamin B<sub>1</sub> in doses of 100 mg., but no improvement was noted in the gangrene, ulcers or objective neurologic changes. Maintenance doses of 20 to 100 mg. once or twice weekly were found necessary to keep the patient free from pain.—M. Naide, *Amer. J. med. Sci.*, 1939, 197, 766.

**NEURITIS in pregnancy.** Four cases successfully treated by oral administration of tablets, each containing 150 units of vitamin B<sub>1</sub>, the dosage being from 10 to 15 tablets daily.—G. W. Theobald, *Lancet*, i/1936, 834.

**TRIGEMINAL NEURALGIA.** Of 7 patients treated with thiamin chloride 6 obtained relief. Four patients who were completely relieved received 160, 210, 84 and 90 mg. each, and in all of them improvement commenced promptly.—I. Bakhsh, *Indian med. Gaz.*, 1939, 456.

**VARICOSE ULCERS.** Of 10 patients with painful varicose ulcers treated with vitamin B<sub>1</sub>, all but one were definitely relieved of pain and 8 had complete subsidence of their symptoms; in 2 cases the symptoms completely subsided in 4 days. In 5 of the cases there was, in addition, definite improvement in the healing of the ulcer. Large doses are necessary, at least 5 mg. (1500 units) 3 times daily by the mouth, and this dose doubled if symptoms do not subside in 3 or 4 days.—A. Ochsner and M. C. Smith, *J. Amer. med. Ass.*, i/1940, 947.

### **Pulvis Vitamin B<sub>1</sub> (B.P. Add. I).** Adsorbate of vitamin B<sub>1</sub>.

**Dose.**—Prophylactic, 15 to 30 grains (1 to 2 g.), equivalent to 100 to 200 units per day. Therapeutic, 30 to 90 grains (2 to 6 g.), equivalent to 200 to 600 units.

The adsorbate on fuller's earth of the antineuritic vitamin, vitamin B<sub>1</sub>, containing 100 units of antineuritic activity per g. It is a cream-coloured, tasteless, odourless powder, insoluble in water or acids.

**Befortiss (Vitamins Ltd., London).** Ampoules contain 2, 10 or 20 mg. of vitamin B<sub>1</sub>, and tablets contain 200 i.u. per g. and 666 i.u. per g. of B<sub>1</sub>, and other factors of the vitamin B complex.

**Bekailin Brand Vitamin B<sub>1</sub> (Vitamins Ltd., London).** Tablets (0.5 g.) of vitamin B<sub>1</sub> concentrate, each containing 100 i.u.

**Bemax (Vitamins Ltd., London).** A stable preparation of wheat germ, standardised to contain 12–15 international units of vitamin B<sub>1</sub> per g., also 3 international units of vitamin A per g., the factors of the vitamin B<sub>2</sub> complex and a high proportion of vitamin E. For constipation, arthritis and conditions of vitamin B<sub>1</sub> deficiency, also in pregnancy and lactation.

**Benerva (Roche Products, Welwyn Garden City).** Preparations of vitamin B<sub>1</sub> available in tablets (1 mg.), and ampoules (2 or 10 mg.).

**Berin (Glaxo Laboratories, London).** Crystalline vitamin B<sub>1</sub>. Ampoules contain 2 mg. in 1 ml. Forte Ampoules contain 10 mg. in 1 ml. Tablets contain 1 mg.

**Betabion (Merck, Darmstadt; Savory & Moore, London).** Pure crystalline vitamin B<sub>1</sub> in tablets each containing 1 mg.; ampoules containing 2 mg. in 1 ml., and ampoules ("strong") containing 10 mg. in 1 ml.

**Betalin 1 (Lilly, London).** Capsules of vitamin B<sub>1</sub> containing 125 i.u. per capsule.

**Betalin S** (*Lilly, London*). Synthetic vitamin B<sub>1</sub> in tablets and ampoules.

**Betalin Compound** (*Lilly, London*). Capsules containing 0.5 mg. of vitamin B<sub>1</sub> and 40 Sherman units of vitamin B<sub>2</sub> from a liver-stomach concentrate.

**Betaxan** (*Bayer Products, London*). Ampoules containing synthetic vitamin B<sub>1</sub>, 1 ml. containing 2 or 10 mg. of the vitamin. Also available in tablets containing 1 mg.

**Crysto-Vibex** (*Parke, Davis, London*). Crystalline vitamin B<sub>1</sub> supplied in tablets containing 0.5 mg. and 1 mg., and in ampoules containing 6.7 mg. in 1 ml.

**Davitamon B<sub>1</sub>** (*Organon Laboratories, London*). Tablets, each containing 1 mg. of aneurin, and 1 ml. ampoules, each containing 2 mg. of aneurin. **Davitamon B<sub>1</sub> Forte**. 1 ml. ampoules, each containing 10 mg. of aneurin.

**Dibexin Capsules** (*Parke, Davis, London*). A combination of aneurin 1 mg. (333 i.u.), vitamin B<sub>2</sub> (riboflavin) 40 Sherman units, with B<sub>3</sub>, B<sub>4</sub>, B<sub>5</sub> and B<sub>6</sub> and nicotinic acid. Advocated for the treatment of deficiencies of vitamins B<sub>1</sub> and B<sub>2</sub>. **Dose**.—As a dietary supplement 1 to 3 capsules daily. Up to 10 daily may be taken in severe vitamin B<sub>1</sub> deficiency. In atonic constipation the dose is 2 to 6 capsules daily.

**Ryzamin-B** (*Burroughs Wellcome, London*). A concentrate of rice polishings, supplied in tubes containing not less than 80 i.u. of vitamin B<sub>1</sub> per g.

**Syrup Vitafruct** (*Thackray, Leeds*). Contains in each fl. dr. 0.33 mg. of vitamin B<sub>1</sub>, 3 fl. dr. representing 500 i.u. **Dose**.—3 fluid drachms daily.

**Riboflavin**. *Syn.* VITAMIN B<sub>2</sub>, LACTOFLAVIN, VITAMIN G.

**Dose**.—2 to 3 mg.

Riboflavin occurs as an orange-yellow crystalline substance, which is *soluble* in water, producing solutions which have a green fluorescence, but is insoluble in chloroform, ether and other fat solvents. It is relatively highly heat-stable. The flavines are a group of yellow water-soluble pigments widely distributed in nature. Riboflavin was first obtained from milk, and on that account is often referred to as lactoflavin. It has been obtained from a large number of natural sources, including such substances as egg albumin, egg yolk, milk, liver, malted barley and yeast.

**Uses**. Although animal experiments indicate that riboflavin is an essential to growth, no therapeutic claims have so far been advanced on its behalf.

**Acidum Nicotinicum** (*U.S.P. XI Supp. II*). *Syn. and Prop. Name*. P.P. FACTOR, PELONIN (*Glaxo Laboratories, London*) (tablets and ampoules each contain 50 mg.).

$C_5H_4N \cdot COOH = 123.1$ .

**Dose**.—Average daily dose 5 grains (0.3 g.).

Nicotinic acid or pyridine- $\beta$ -carboxylic acid is a product of the oxidation of nicotine. It is obtained synthetically and occurs in colourless, odourless crystals melting at 234° to 237°.

**Soluble** about 1 in 60 of cold water; freely soluble in hot water and hot alcohol; insoluble in ether.

**Uses**. Nicotinic acid is either the pellagra-preventive vitamin, or a pro-vitamin, or it may be conjugated with other substances in the body into a more complex compound that is essential to counteract pellagra. Nicotinic acid is used in the treatment of acute pellagra, causing the disappearance of the characteristic lesions of the disease, a greatly improved mental condition and a normal porphyrin content of the urine. Chronic cases do not

respond so well. It does not affect the polyneuritis often associated with pellagra and such cases require the administration of aneurine. Nicotinic acid has also been employed in the treatment of acrodynia, sprue, and some forms of glossitis and stomatitis.

**DELIRIUM TREMENS.** In a chronic whisky addict an attack of delirium tremens (recurrence) associated with severe gastro-intestinal manifestations and acute stomatitis was made to disappear within 12 hours by the administration of nicotinic acid (0.5 g.). Previous to this thiamin had been given in large doses but without perceptible result.—F. Mainzer and M. Krause, *Brit. med. J.*, ii/1939, 331.

**PELLAGRA.** Elvehjem has shown that nicotinic acid or its amide (isolated from liver) has a curative effect on blacktongue in dogs and it has since been found at the Cambridge Nutritional Laboratory that nicotinic acid has a curative action on monkey pellagra due to a diet deficient in the P-P (pellagra-preventing) factor. Trials on 5 human pellagrins using up to 0.33 g. daily showed in all cases that nicotinic acid exerted a curative effect on the erythema but had less effect on the general condition of the patients. It is suggested that either human pellagra is due to a deficiency of more than one factor or nicotinic acid may be the precursor of the P-P factor which is formed from it in the body.—L. J. Harris, per *Lancet*, ii/1937, 1467.

Studies on 15 pellagrins showed the administration of nicotinic acid is followed promptly by remission of the pellagrous glossitis, stomatitis, ptialism, vaginitis, urethritis, and porphyrinuria. None of these manifestations of pellagra returned so long as the patient continued to take the nicotinic acid, even though he ate only a basic diet, but they returned if he continued to take only a pellagra-producing diet and did not take nicotinic acid. The suggested safe and effective dose is 0.5 g. per day in five doses of 100 mg. each, or it may be given parenterally in a dose of 10 to 20 mg. in sterile physiological saline four times a day. Its use should be combined with a well-balanced diet.—T. D. Spies, *Lancet*, i/1938, 252. See also *J. Amer. med. Ass.*, i/1938, 622.

Thirteen cases of endemic pellagra responded promptly to nicotinic acid therapy. The most striking effect was the rapid healing of lesions of the alimentary tract with development of an excellent appetite and gastrointestinal function and the spectacular disappearance of mental symptoms. It does not seem to be effective against the peripheral neuritis associated with pellagra, which is improved, however, by large doses of synthetic vitamin B<sub>1</sub>, intravenously and intraspinally.—R. S. Matthews, *J. Amer. med. Ass.*, ii/1938, 1148. See also T. D. Spies *et al.*, *ibid.*, 584.

**RADIATION SICKNESS.** Results from nicotinic acid therapy (200 mg. 3 times daily) would appear to be better than from Nembutal or intramuscular liver. Ease of administration with no unpleasant after effects is definitely advantageous.—J. W. Graham, *J. Amer. med. Ass.*, ii/1939, 664.

**VINCENT'S DISEASE.** Four cases of severe Vincent's disease successfully treated by nicotinic acid by mouth, 250 mg. daily dissolved in water.—J. D. King, *Lancet*, ii/1940, 32.

**Nicotinic Acid Amide.** *Syn.* NICOTINAMIDE.  
 $C_6H_7N \cdot CONH_2 = 122.1$ .

**Dose.**—Average daily dose 5 grains (0.3 g.).

Nicotinic acid amide occurs as white, odourless, needle-like crystals with a bitter taste. M.p. 133°.

**Soluble** in water, alcohol and benzene; insoluble in ether.

**Uses.** May be used similarly to nicotinic acid in the treatment of pellagra.

15 patients with pellagra and dermatitis, and 2 with pellagrous stomatitis were treated with nicotinamide (1 g. by mouth or 0.5 g. by injection daily), meat and milk being cut off as soon as treatment was begun. Nicotinamide effected great improvement in the acute mucous membrane lesions and a slower improvement in the acute skin conditions. The appetite, mental condition and general physical health of all the patients were improved.—A. C. Alport, *Lancet*, ii/1938, 1460.

**Pyridoxin.** *Syn.* VITAMIN B<sub>6</sub>, ADERMIN. C<sub>8</sub>H<sub>11</sub>NO<sub>3</sub> = 169.2.

*Dose.*—50 to 100 mg. subcutaneously at weekly intervals.

Pyridoxin is 2-methyl-3-hydroxy-4:5-(hydroxymethyl)-pyridine, occurring in yeast, liver, rice bran, etc., and prepared synthetically. White crystals, m.p. 160° (with decomposition).

**Soluble** in water, alcohol and acetone; less soluble in chloroform and ether.

**Uses.** The available evidence indicates that pyridoxin is an important factor in nutrition, and deficiency may give rise to a symptom complex in which muscular weakness and rigidity are prominent. It has been employed with some success in a small number of patients in myasthenia gravis, in muscular dystrophy and in paralysis agitans.

**ANÆMIA.** When administered in large amounts, has a definite effect upon the hæmopoietic system of human beings who have macrocytic anæmia of pellagra or pernicious anæmia in relapse. This substance does not, however, act specifically either as the true anti-pernicious factor or as the extrinsic factor of Castle.—R. W. Viller, H. S. Schiro and T. D. Spies, *Nature, Lond.*, i/1940, 388.

**MUSCULAR DYSTROPHY.** Used in six cases of pseudo-hypertrophic muscular dystrophy with considerable improvement.—W. Antopol and C. E. Schotland, *J. Amer. med. Ass.*, i/1940, 1058.

**PARKINSONISM.** Definite improvement in all of three post-encephalitic cases and in two out of eight arteriosclerotic cases.—T. D. Spies *et al.*, *J. Amer. med. Ass.*, ii/1940, 294.

## ANTIMONIUM

Sb = 121.76.

[P1] "*Antimony, chlorides of; oxides of antimony; sulphides of antimony; antimonates; antimonites; organic compounds of antimony.*"

[S1] "*Antimonial poisons except substances containing less than the equivalent of one per cent. of antimony trioxide.*"

[S3] "*Antimony, chlorides of—in polishes.*"

[S6] "*Antimonial poisons—specify proportion as the proportion of antimony trioxide (Sb<sub>2</sub>O<sub>3</sub>) or antimony pentoxide (Sb<sub>2</sub>O<sub>5</sub>) that the preparation would be calculated to contain on the assumption that the antimony (Sb) in the poison had been wholly converted into antimony trioxide or antimony pentoxide as the case may be.*"

**Antidotes to Antimony Salts.** Give emetic if vomiting has not occurred and wash out stomach with 180 gr. of tannic acid in 2 gallons of water, using stomach tube. Give 20 gr. of tannic acid in water and repeat 5 gr. doses every  $\frac{1}{2}$  hour for 4 or 5 doses. Keep patient warm and give demulcent drinks. Strychnine,  $\frac{1}{4}$  gr., hypodermically. Saline infusion may be necessary. Morphine,  $\frac{1}{4}$  gr., hypodermically, in cases of extreme irritability.

[P1-S1] **Antimonii Oxidum (B.P.C.).** ANTIMONIOUS OXIDE.

Sb<sub>2</sub>O<sub>3</sub> = 291.5.

*Dose.*—1 to 2 grains (0.06 to 0.12 g.).

A white powder, *soluble* in hydrochloric acid and in alkaline tartrate solution, caustic alkalis, etc. Diaphoretic, expectorant and emetic.

[P1-81] **Pulvis Antimonialis (B.P.C.).** *Syn.* JAMES'S POWDER.

*Dose.*—3 to 6 grains (0.2 to 0.4 g.).

Contains 33½% of antimonious oxide in calcium phosphate.

[P1-81] **Antimonii Trichloridum (Fr. Cx.).** ANTIMONIOUS CHLORIDE.  $\text{SbCl}_3 = 228.1$ . A colourless, crystalline mass. M.p. 73°. It is very corrosive and hygroscopic, hence **butter of antimony** is usually liquid; on addition of water it decomposes into free hydrochloric acid and basic antimony oxychloride. A solution of pure antimonious chloride in chloroform is used as a test for vitamin A.

[P1-81] **Liquor Antimonii Chloridi (B.P.C.).** *Syn.* BUTTER OF ANTIMONY. A solution of antimonious chloride containing 17 to 18% w/w of Sb. Formerly used as an escharotic, now used mainly in veterinary practice and in furniture polishes.

[P1-81] **Antimonii et Potassii Tartras (B.P., U.S.P. XI, F.E. VIII, P. Belg. IV, P. Helv. V, P. Dan., and P. Ital. V).** *Syn.* POTASSIUM ANTIMONYL TARTRATE, TARTAR EMETIC, ANTIMONIUM TARTARATUM, TARTARATED ANTIMONY, ANTIMONY AND POTASSIUM TARTRATE, EMÉTIQUE (Fr. Cx.).

$\text{C}_4\text{H}_4\text{O}_7\text{SbK}, \frac{1}{2}\text{H}_2\text{O} = 333.9$ .

*Dose.*—Diaphoretic and expectorant  $\frac{3}{16}$  to  $\frac{1}{8}$  grain (0.002 to 0.008 g.), emetic  $\frac{1}{2}$  to 1 grain (0.03 to 0.06 g.). *Intravenously*  $\frac{1}{2}$  to 2 grains (0.03 to 0.12 g.), usually in 1 or 2% solution. *Hypodermically* it is painful, irritating and *not advised*, and *intramuscularly* it is too painful.

*Fr. Cx.* has max. single dose 1 grain; max. in 24 hours 3 grains. *P. Helv. V* max. in 24 hours  $4\frac{1}{2}$  grains.

A single dose over limit of safety, *i.e.*, between 0.01 and 0.02 g. per kilo weight, is sufficient to cause death.

Asphyxia in a woman following 1 grain in 6% solution intravenously. Recovery after intracardiac injection of 0.2 ml. of 1 in 1000 adrenaline.—*Lancet*, ii/1931, 1325.

Made by combining antimonious oxide with potassium acid tartrate. It occurs in colourless crystals or as a white powder.

**Soluble** 1 in 17 of cold water, 1 in 3 of boiling water and 1 in 20 of glycerin. Almost insoluble in alcohol 90%.

**Incompatible** with acids and alkalis, soap, and tannin.

**Uses.** Diaphoretic and emetic when given orally. In sub-emetic doses it is an active remedy in acute bronchitis, often given in combination with opium. It is mainly used for the intravenous administration of antimony in the treatment of cutaneous leishmaniasis, frambæsia, filariasis, schistosomiasis, espundia, kala-azar and oriental sore. Is also beneficial in relapsing fever and has been given with benefit in cerebrospinal fever. Is almost specific in granuloma inguinale, and has proved of value in the treatment of trypanosomiasis in cattle.

For schistosomiasis and kala-azar it is commonly given as a 2% solution in initial doses of  $\frac{1}{2}$  gr., increasing at each injection by  $\frac{1}{2}$  gr. to a maximum of 2 gr. The injections are given on alternate

days or twice weekly until 25 to 30 gr. has been given. During the course of the injections, red blood first disappears from the urine although smokiness remains until about 20 gr. has been given. Injections should be given only with great caution if there is any lesion of the heart, lungs, kidneys or liver. In the treatment of schistosomiasis it has also been employed rectally; initial dose 1 gr., then 2 gr. every second day, increasing to 3, 4 and 5 gr. during three weeks in 100 ml. of water.

ACNE ROSACEA cured in 5 weeks by tartarated antimony,  $\frac{1}{16}$  gr. *per os* thrice daily after meals, combined with application night and morning of a lotion containing sulphur, zinc oxide and magnesium carbonate. Good results also in furunculosis and ulcerative legs.—L. W. Bain, *Brit. med. J.*, ii/1929, 51.

CHANCROID well treated. 5 ml. of a 1% solution intravenously, every second day or at longer intervals; 4 to 6 injections increased by 1 ml. to a total of 12 ml.

KALA-AZAR. Compulsory treatment in Assam with tartar emetic intravenously "has converted a disease with a 90% mortality into one with a 90% rate of cure."

There is sufficient evidence to demonstrate that antimony is by no means a satisfactory specific for kala-azar in the Sudan, although up to the present time it has been the only drug of any value.—E. S. Horgan and R. Kirk, *Nature*, *London*, i/1940, 228.

KERATITIS has been well treated by tartar emetic intravenously.

SCHISTOSOMIASIS. "Rheumatic pains" liable to occur during the night following the 4th or 5th injection. There is increased hæmaturia as treatment proceeds; later, the blood and the ova vanish. Where there is intolerance, give brandy,  $\frac{1}{2}$  ml. adrenaline solution and  $\frac{1}{2}$  ml. post-pituitary extract intramuscularly.

In bilharzia its use is generally accompanied by cough, vomiting, and fainting.—M. Khalil and M. H. Betache, *Lancet*, i/1930, 234.

Exceeding the maximum dose causes sudden displacement of the bilharzia parasites, which lose their hold on the vein-walls and are precipitated as thrombi into the liver, possibly resulting in hepatitis, congestion of the bile ducts, or even septic foci in the pulmonary circulation, if not completely destroyed. The method of choice is gradual destruction over a period of one month.—F. G. Cawston, *J. trop. Med. (Hyg.)*, Feb. 16, 1931.

TRACHOMA. The corneal complications of trachoma which respond poorly to the usual methods of treatment show distinct improvement following the intravenous injection of 1% tartar emetic. The dose is 5 ml. on 6 successive days, 10 ml. on the 8th day and this dose repeated on the 10th, 12th, 15th, 19th, 22nd, 25th, 28th and 31st days of treatment, or a total of 1.2 grammes in 31 days. The treatment may be supplemented by painting the fornices with the 1% solution once a day and instilling drops of the same strength three times a day. If more than a small quantity of the drug escapes into the subcutaneous tissues severe local reactions may occur. Muscular stiffness is a not uncommon complication in the later stages of treatment; it is felt in the mornings but wears off during the day.—Julianelle *et al.*, *per Brit. med. J.*, i/1939, 516.

TUBERCULOUS HÆMOPTYSIS may be arrested with tartar emetic by the mouth—a total daily dose of 0.05 to 0.15 g., usually for 5 days, in pills containing 0.02 to 0.05 g. with 0.01 g. of opium, with water an hour before or after meals.

TRYPANOSOMIASIS IN CATTLE. Of value in *T. congolense* or *T. vivax* infections—1 g. intravenously every 3 days for 6 doses. Of no value in horses infected with *T. brucei*.—Wenyon, *p.* 462. Successful in saving the lives of thousands of animals.—Ll. E. W. Bevan, *Trans. R. Soc. trop. Med. Hyg.*, Aug., 1923, 154.

After a single course of tartar emetic injections relapses to *T. vivax* infection are the exception, whereas relapses to *T. congolense* infection are the rule.—H. E. Hornby, *Trans. R. Soc. trop. Med. Hyg.*, Jan., 1929, 403; also J. N. Hall, *ibid.*

Following the use of the injections (in Swaziland) abscess formation round the injected jugular vein is very common, the injections often being attempted by the farmers themselves who rely on distilled rather than boiled water for making the solution. To control any local reaction from unskilful injections of stock infected with nagana it is recommended that the powder be dissolved in a

1 or even 2% solution of phenol and a little glycerin added.—F. G. Cawston, *J. trop. Med. (Hyg.)*, 1935, 306.

[P1] **Hausus Emeticus Purgans** (*Mid. H.*).

Potassium antimonyltartrate  $\frac{1}{2}$  gr., magnesium sulphate 60 gr., water to 1 oz. for a dose.

[P1] **Vinum Antimoniale** (*B.P.C.*, *P. Ned. V*, *I.A.*).

*Dose*.—10 to 30 minims (0.6 to 2 ml.); as emetic 2 to 4 drachms (8 to 15 ml.).

Contains 1 in 250 of potassium antimonyltartrate in sherry-type wine.

Pneumonia has been treated by repeated  $2\frac{1}{2}$  minim doses of antimonial wine. Crisis comes at the end of the fourth day.

HEADACHE DUE TO HIGH BLOOD PRESSURE. Especially of value where chronic interstitial nephritis is a contraindication to blue pill.—A. Feiling, *Brit. med. J.*, ii/1930, 907.

[P1] **Mist. Antimon.** (*N.I.F.*). Antimonial wine 5 m., potassium nitrate 10 gr., strong solution of ammonium acetate 30 m., camphor water to  $\frac{1}{2}$  oz.

[P1] **Mistura Vini Antimonialis** (*St. J. H.*).

Magnesium sulphate 20 gr., antimonial wine 10 m., water to  $\frac{1}{2}$  oz.

Will give very gratifying results in the early stages of many inflammatory diseases such as psoriasis or lichen planus.—J. E. M. Wigley, *Practitioner*, 1935, 359.

[P1-S1] **Unguentum Tartari Stibiati** (*P. Ital. V*).

Potassium antimonyltartrate 20 g., lanolin or soft paraffin 80 g.

[P1-S1] **Antimonii et Sodii Tartras** (*B.P.*). *Syn.* SODIUM ANTIMONYLTARTRATE.  $C_4H_4O_7SbNa = 308.8$ .

*Dose*.—As for Antimonii et Potassii Tartras.

*Caution*. One-third of the amount of antimony injected is excreted by the kidneys in 24 hours. Great caution is required where heart, kidney or lung disease exists. In weak, emaciated and anæmic subjects begin with small dose gradually increased.

In colourless, hygroscopic scales or powder with sweetish taste.

*Soluble* 1 in  $1\frac{1}{2}$  of water; insoluble in alcohol.

*Uses*. This compound has properties similar to those of tartar emetic. Its greater solubility may be of some advantage and it is considered to be less irritant and less toxic than the potassium compound. It has been largely employed in schistosomiasis and in oriental sore and kala-azar in the same dosage as potassium antimonyltartrate.

Antimony sodium tartrate is less toxic and irritant than tartar emetic. It can be sterilised by boiling and the following method is used. The drug is weighed out, dissolved in more than the required volume of water and filtered into a flask graduated to the required volume. It is then sterilised by gently boiling down to the graduation mark.—O. Turner, *Trans. R. Soc. trop. Med. Hyg.*, 1940, 34, 111.

[P1-S1] **Antimonium Sulphuratum** (*B.P.C.*).

*Dose*.—1 to 2 grains (0.06 to 0.12 g.).

A mixture of the sulphides and oxides in orange red powder.

*Uses*. Alterative and emetic, but uncertain in action. Has been used in conjunction with calomel and guaiacum and resin in the treatment of gout and rheumatism (Plummer's Pills).

[P1-S1] **Kermes Minerale** (*Fr. Cx.*, *P. Belg. IV*) is made by boiling black antimony sulphide (trisulphide) with sodium carbonate solution, and allowing the liquor to cool. [P1-S1] **Tabletæ Kermetis** (*P. Belg. IV*) contain 0.01 g.

*Dose*.—1 to 2 grains. *Incompatible* with acids, sodium bicarbonate and potassium acid tartrate.

[P1-S1] **Antimonii Pentasulphidum** (*P. Ned. V, P. Belg. IV, P. Ital. V, P. Helv. V, P. Dan.*).  $\text{Sb}_2\text{S}_3 = 403.82$

An orange powder made by decomposing Schlippe's salt (sodium sulph-antimonate,  $\text{Na}_3\text{SbS}_6 \cdot 9\text{H}_2\text{O}$ ) with dilute sulphuric acid.

[P1-S1] **Antimonium Nigrum Purificatum** (*P. Belg. IV, P. Helv. V*).  $\text{Sb}_2\text{S}_3 = 339.7$ .

Greyish crystalline powder obtained by purification of native antimony sulphide. Decomposed by boiling hydrochloric acid. Used in veterinary practice as parasiticide.

[P1-S1] **Stibium Sulfuratum Depuratum** (*Fr. Cx.*).  $\text{Sb}_2\text{S}_3$ . Grey, crystalline substance; sp. gr. about 4.6; m.p.  $540^\circ$ . It is used for making Kermes Minerale (*Fr. Cx.*).

[P1-S1] **Stibium Sulfuratum (Trisulfuro) Crudum**. *Syn.* STIBINA OR ANTIMONIO CRUDO (*P. Ital. V*) is converted into [P1-S1] **Stibium Sulfuratum depuratum**, *syn.* STIBINA DEPURATA, by treatment with ammonia. *F.E. VIII* is similar.

[P1-S1] **Antimony Crocus**. For veterinary use, is a mixture of trioxide (about 4 parts) and trisulphide (1 part). Formed by heating equal weights of antimony trisulphide and potassium nitrate to which  $\frac{1}{2}$  of hydrochloric acid has been added.

**Colloidal Antimony** has been given intramuscularly in leprosy, leishmaniasis, and pulmonary tuberculosis.

[P1-S1] **Stibophenum** (*B.P. Add. III*). *Prop. Name.* FOUADIN (*Bayer Products, London*).  $\text{C}_{12}\text{H}_4\text{O}_{16}\text{S}_4\text{SbNa}_5 \cdot 7\text{H}_2\text{O} = 895.1$ .

*Dose.*— $1\frac{1}{2}$  to 5 grains (0.1 to 0.3 g.), by intravenous injection.

Similar dosage is employed intramuscularly.

Sodium - antimony - bispyrocatechol - 3:5 - sodium disulphonate, containing about 15.8% of antimony. It is a colourless, odourless, crystalline powder.

Freely **soluble** in water; almost insoluble in organic solvents. Aqueous solutions are at first colourless, but gradually turn lemon-yellow in colour. The formation of the yellow colour may be prevented by the addition of acid.

**Uses.** Stibophen is employed principally in the treatment of schistosomiasis, usually in the form of a 6.3% solution. A dose of 1.5 ml. of this solution is given intramuscularly on the first day, 3.5 ml. on the second day, and 5 ml. on the third day and every other day, to a total of 40 to 75 ml. A similar scheme of dosage may also be employed with success in the treatment of undulant fever and oriental sore. It is rapidly effective, especially when given in conjunction with sulphanilamide (0.5 g. five times daily for 5 days, and then four times daily for 3 days), in granuloma inguinale.

Although it is much less toxic than tartar emetic and seldom gives rise to local complications, toxic symptoms such as nausea, epigastric pain, giddiness and vomiting are occasionally experienced. It is also cumulative in action and may have a deleterious effect on the liver if the course of treatment is too prolonged.

*Test for excretion.* In schistosomiasis, although the majority are cured, there are some resistant cases that need prolonged treatment, while there are others (a very few) which cannot tolerate the drug. The drug is excreted mainly through the kidneys and it has been found that the amount and rate of excretion differs greatly in different persons, and patients who excrete the drug very quickly belong to the class that are not cured by the ordinary course of treatment, whereas those who excrete the drug very slowly are those that readily show symptoms of



intolerance. The test is as follows: To 5 ml. of the urine add 5 ml. of a fresh 0.05% solution of  $\text{FeCl}_3$  and make the mixture alkaline by adding strong ammonia. A red colour indicates the excretion in some form of the drug. The depth of colour is found to correspond approximately to the amount of antimony in the urine as revealed by the Reinsch test. The excretion of antimony continues, however, after the colour-test has become negative. By means of this test it is possible to test indirectly the excretion of antimony after the first injection, and to adjust the dose according to the results—increasing it for quick excretors and reducing it for slow excretors.—M. Khalil, *Lancet*, ii/1936, 132.

**DISSEMINATED SCLEROSIS.** A course of 10 or 12 intramuscular injections is often very helpful.—Macdonald Critchley, *Med. Pr.*, i/1936, 520.

**GRANULOMA INGUINALE.** A safe and rapid specific. Generally superior to potassium antimoniyttartrate and without dangerous reactions.—*J. Amer. med. Ass.*, i/1933, 1674.

**SCHISTOSOMIASIS** cured by intramuscular injections of 1 to 5 ml. of 7% solution. Local reaction slight, and no deaths or serious symptoms occurred in 20 cases. 2 weeks treatment gives cure.—*Brit. med. J. Egit.*, ii/1929, 92.

**Schistosomiasis** in W. African children. Given intramuscularly, the total course of treatment being equivalent in ml. to the weight of the child in kilos; given in 10 doses, the third to the tenth being equal and given on alternate days; the first injections given on consecutive days and being about 30% and 70% respectively of succeeding full doses. Of 6 cases treated all were clear of ova by the twenty-fourth day, but there was loss of weight and considerable local pain.—R. M. Gordon and E. P. Hicks, *Ann. trop. Med. Parasit.*, Oct. 22, 1930.

Nine intramuscular injections for an adult cure in the majority of cases. First day, 1.5 ml.; second, 3.5 ml.; third, 5 ml.; fifth, 5 ml.; seventh, 5 ml.; ninth, 5 ml.; eleventh, 5 ml.; thirteenth, 5 ml.; fifteenth, 5 ml. If ova found give further two doses.—M. Khalil and M. H. Betache, *Lancet*, i/1930, 234.

Because of its inferior antimony content it cannot be recommended in the treatment of schistosomiasis except where intravenous injections are impossible and where treatment can be repeated if found necessary.—F. G. Cawston, *J. trop. Med. (Hyg.)*, 1936, 29.

**UNDULANT FEVER.** Eight cases at Malta successfully treated by intramuscular injection of 1.5 ml. on the first day, 3.5 ml. on the second day, followed by 5 ml. on alternate days. As a result of the injections, there were no waves of fever after the first, though such waves are one of the characteristics of the disease.—C. Z. Neumann, *Lancet*, i/1936, 1001.

[P1-81] **Anthiomaline** (*Pharmaceutical Specialities (May & Baker) Ltd., London*). Lithium antimony-thiomalate. An organic compound containing 16% of antimony. *Dose*.—From 0.5 to 2 ml. (1 ml. = 0.01 g. Sb) intramuscularly, for a course of 12 to 20 injections, at the rate of 2 or 3 a week. In lympho-granuloma inguinale, schistosomiasis and leishmaniasis. Has low toxicity and is well tolerated.

**SCHISTOSOMIASIS.** 2 ml. of Anthiomaline is a sufficiently large repeated dose for a child, and 4-ml. doses should not be exceeded in adults. Excessive doses cause salivation or retching. A cure may sometimes be obtained in less than the month usually required with tartar emetic.—F. G. Cawston, *Prescriber*, 1936, 233.

[P1-81] **Neostam** (*Burroughs Wellcome, London*). A brand of stibamine glucoside (the nitrogen-glucoside of sodium *p*-aminophenylstibonate) available in phials of 0.05, 0.1, 0.2, 0.5 and 1 g. for use in kala-azar, etc. *Dose*.—0.1 g. per 100 lb. body weight intravenously as a 4% solution in distilled water on alternate days until 3 g. per 100 lb. b/w has been given.

[P1-81] **Neostibosan** (*Bayer Products, London*). *Syn.* "693 B." Diethylamine-*p*-aminophenyl stibinate. In kala-azar. *Initial dose*.—0.05 to 0.02 g. according to age intravenously; 8 injections on 8 consecutive days for intensive treatment.—*See also Brit. med. J. Egit.*, i/1931, 65.

**KALA-AZAR.** It has been shown by Napier that the treatment of all cases in Bengal villages with Neostibosan has been followed in a few years by the disappearance of the disease.—*Trop. Dis. Bull.*, 1940, 350.

**MEDITERRANEAN VISCERAL LEISHMANIASIS.** The pentavalent preparations have attained their maximum effect and most convenient form in Neostibosan. With tartar emetic and Neostibosan almost 100% of cures have been obtained during the last few years. Contraindications are profound renal lesions and serious

cardiac disorders.—Caronia (Italy). Neostibosan has yielded excellent results.—Sergent (Algeria). Results with Neostibosan highly favourable—70% of cures.—Pitaluga (Spain).—*Quart. Bull. Hlth Org. L.o.N.*, Dec., 1935, 801.

[P-81] **Urea Stibamine** (*Brahmachari Institute, Calcutta; Pharmaceutical Products, London*) is composed of urea and *p*-aminophenylstibinic acid,  $\text{NH}_2\text{C}_6\text{H}_4\text{SbO}(\text{OH})_2$ , but apparently not a definite compound.

Safer than tartar emetic in the treatment of kala-azar. Intravenous injections on alternate days, starting with 0.1 g. in cold sterile water, increasing by 0.05 g. to a maximum of 0.25 g. and continued for subsequent doses. Rapidity of disappearance of symptoms compared with sodium antimonyl tartrate, 2 to 3 weeks as against 3 months.

It has been shown (Gray *et al.*, *Proc. R. Soc. Med.*, B, 1931, 108, 54) that the effective active principle of Urea Stibamine is S-diphenylcarbamide-4:4-distibinic acid, which is rendered water-soluble in the presence of protective colloids, and that the analysis of Urea Stibamine gives fairly constant results. The conclusions of early workers that the so-called Urea Stibamine varied widely in its antimony content and was uncertain in its composition are therefore erroneous, and due to the fact that various products were marketed which did not conform to the original specification.—U. Brahmachari, *Nature, Lond.*, i/1940, 1021.

It was found at the Peiping Union Medical College that an adequate course of Urea Stibamine (in kala-azar) for a child was 1.0 to 1.5 g., as contrasted with 1.5 to 2.5 g. for Neostibosan. For an adult the figures were 1.5 to 2.5 g. and 4.0 to 5.0 g. Urea Stibamine is thus definitely more potent than Neostibosan, which, on the other hand, has the advantage of being a definite chemical compound of a lower toxicity. After treatment with either of these drugs patients must be followed for at least 7 months to a year before cure can be pronounced.—C. U. Lee and C. F. Chu, *Chinese med. J.*, 1935, 328.

## APIOL

*B.P.C., P. Belg. IV, Fr. Cx.*

**Dose.**—3 to 10 minims (0.2 to 0.6 ml.), in perles, 3 minims in each, or capsules 3, 5 and 10 minims in each.

Apiol is obtained by alcoholic extraction from the fruit of *Carum Petroselinum*, syn. *Apium Petroselinum*, *Petroselinum sativum*, common parsley. The alcohol is evaporated and the residue allowed to cool, the clear liquid being decanted. It is a green oil, with a peculiar odour and a pungent taste like parsley. Sp. gr. 1.055 to 1.091.

**Soluble** readily in alcohol and ether.

Apiol is claimed to be efficacious in primary amenorrhœa or deficiency of secretion, as well as in dysmenorrhœa. It is given night and morning for 4 or 5 days during the period.

The Inter-Departmental Committee on Abortion recommended the inclusion of apiol in the Fourth Schedule.—*Report of the Inter-Departmental Committee on Abortion, H.M.S.O.*, 1939.

**Toxic Effects.** Clinical observations on 37 women with toxic polyneuritis following the use of apiol as an abortifacient.—R. Carrillo and J. W. G. T. Braak, per *J. Amer. med. Ass.*, ii/1932, 698.

Polyneuritis frequently follows its administration. Due to tri-ortho-cresyl phosphoric acid of which apiol contains 28 to 50%.—*Brit. med. J. Ept.*, i/1933, 12.

Three cases of polyneuritis following use of apiol as an abortifacient, due to the presence in it of tri-ortho-cresyl phosphate.—J. J. Waite, per *Brit. med. J. Ept.*, ii/1933, 5.

**TRI-ORTHO-CRESYL PHOSPHATE.** The use of this compound in the preparation of a synthetic ginger extract, caused an epidemic of peripheral motor paralysis of the legs and arms. 20,000 cases of paralysis due to the drinking of this imitation ginger extract occurred in the South-East of the United States in 1930 before the cause was discovered. Very few deaths resulted, but partial recovery occurred

only after some months, and in many cases the paralysis seems permanent. This paralysis is only produced by tri-ortho-cresyl phosphate: it is not produced by ortho-cresyl, or by para- or meta-tri-cresyl phosphate.—*Brit. med. J.*, ii/1933, 579.

[P1-S1] **Capsules of Apiol and Ergotin.**

Contain apiol 5 minims (0.3 ml.) and extract of ergot 2 grains (0.12 g.).

[P1-S1] **Ergoapiol** (*Martin H. Smith, New York; Christy, London*). Capsules containing ergot extract 0.065 g., aloin 0.008 g., oil of savin 0.03 g., and apiol 0.3 g. For amenorrhœa, dysmenorrhœa and allied disorders.

A fatal case of poisoning in a young woman who took 17 of the capsules to induce abortion.—K. Lowenberg, *J. Amer. med. Ass.*, i/1938, 573.

**Oleum Petroselinii** (B.P.C.). *Syn.* OIL OF PARSLEY.

*Dose.*—3 to 5 minims (0.2 to 0.3 ml.).

The oil distilled from the fruit of parsley, *Carum Petroselinum*. A viscous colourless or yellowish oil, resembling apiol in properties.

“**Green Apiol**” is obtained by extracting the fruits with ether and evaporating the solvent. It has a lower sp. gr. than apiol (about 0.93). This may be purified to yield a viscous, oily, yellow, liquid apiol.

**Apiolum** (F.E. VIII). *Syn.* APIOLE, CRYSTALLINE APIOL, “WHITE APIOL,” ÉTHER MÉTHYLÉNIQUE ET DIMÉTHYLIQUE DE L'ALLYL-APIONAL, CAMPRE DE PERSIL.  $\text{CH}_2\text{O}_2\text{C}_6\text{H}_4(\text{OCH}_3)_2\text{CH}_2\text{CH}:\text{CH}_2 = 222.23$ .

In acicular crystals, slightly soluble in water, readily soluble in chloroform, ether and alcohol 90%. M.p.  $29^\circ$  to  $30^\circ$ .

**Dill-Apiole**,  $\text{C}_{12}\text{H}_{14}\text{O}_4$ , is an isomeric substance obtained from oil of Indian dill (*Anethum Sowa*).

**Apium** (B.P.C.). *Syn.* CELERY FRUIT, CELERY SEED.

*Dose.*—20 to 60 grains (1.2 to 4 g.).

The dried ripe fruits of cultivated plants of celery, *Apium graveolens* (Umbelliferae). Contain 2 to 3% of volatile oil. Nervine sedative and tonic. The decoction (1 in 20) is a domestic remedy for rheumatism. The root is used in “Sirop des Cinq Racines” (*Fr. Cx.*).

**Extractum Apii Liquidum** (B.P.C.). *Dose.*—5 to 20 minims (0.3 to 1.2 ml.). 1 in 1.

**Oil of Celery.** *Dose.*— $\frac{1}{2}$  to 3 minims or more. Capsules are made  $3\frac{1}{2}$  and 5 minims. Contains a small proportion of apiol. Antispasmodic and nerve stimulant. In rheumatoid arthritis 5 to 15 minim doses have been used successfully. It acts probably as an intestinal antiseptic.

## APOMORPHINÆ HYDROCHLORIDUM

B.P., U.S.P. XI, P. *Helv.* V, P. *Jap.* V, P.G. VI, P. *Ned.* V.

$\text{C}_{17}\text{H}_{17}\text{O}_2\text{N}\cdot\text{HCl}\cdot\frac{1}{2}\text{H}_2\text{O} = 312.8$ .

*Syn.* CHLORETUM APOMORPHICUM (P. *Dan.*, P. *Ital.* V, F.E. VIII, P. *Belg.* IV).

[P1] “*Alkaloids, the following; their salts, simple or complex:—Apomorphine.*”

[S1] “*Alkaloids, the following; their salts, simple or complex:—Apomorphine except substances containing less than 0.2% of apomorphine.*”

**Dose.**— $\frac{1}{64}$  to  $\frac{1}{32}$  grain (0.001 to 0.002 g.), increased, as an expectorant;  $\frac{1}{32}$  to  $\frac{1}{8}$  grain (0.002 to 0.008 g.) hypodermically as an emetic and hypnotic. The oral dose as an emetic is  $\frac{1}{10}$  to  $\frac{1}{4}$  gr. (0.006 to 0.016 g.).

A derivative of morphine or codeine obtained by heating them with an excess of hydrochloric acid in sealed tubes. In commerce the hydrochloride occurs in greyish white, acicular crystals which become greenish on exposure to air and light. *Fr. Cx.* has the anhydrous salt.

**Soluble** 1 in 60 of water, 1 in 30 of alcohol 90%. Almost insoluble in ether and chloroform. A trace of acid prevents solutions turning green, *vide* *Injectio postea*.

**Incompatible** with sodium carbonate and bicarbonate, tannin and iron salts.

**Antidotes.** Give repeated  $\frac{1}{2}$ -dr. doses of aromatic spirit of ammonia in water, or ammonia inhalations. Keep patient lying down and warm.

**Uses.** In all cases of non-corrosive poisoning it is of great value as an emetic. It is an anti-stimulant; in bronchial asthma doses of  $\frac{1}{8}$  grain are very useful. Small doses are expectorant and relieve bronchitis and pertussis. In puerperal convulsions it soon causes vomiting and free perspiration; patient sleeps and awakes quiet.

In a case of obstruction of the œsophagus by a plum-stone, the injection of apomorphine hypodermically caused its removal.

#### [P1-S1] **Injectio Apomorphinæ.**

Apomorphine hydrochloride 1, dilute hydrochloric acid 1, distilled water to 100.  $\frac{1}{10}$  gr. in 11 m.

**Dose.**—5 to 10 minims (or more) as an emetic. The addition of the trace of acid keeps it stable and colourless.

The effect produced by a small injection on a mad-drunk patient is remarkable. As hypnotic  $\frac{1}{10}$  to  $\frac{1}{8}$  grain. The patient, however wild, sleeps 12 hours and awakes refreshed.

[D-P1-S1] **Mistura Apomorphinæ Composita.** *Syn.* MISTURA TUSSIS, *Luff.*  
**Dose.**— $\frac{1}{2}$  ounce every 4 hours.

Apomorphine hydrochloride  $\frac{3}{4}$  gr., morphine hydrochloride  $\frac{1}{4}$  gr., diamorphine hydrochloride  $\frac{1}{4}$  gr., dilute hydrochloric acid 5 m., syrup of wild cherry  $\frac{1}{2}$  dr., chloroform water to  $\frac{1}{2}$  oz.

A palatable mixture useful for irritable cough, especially post-influenzal cough. The hydrochloric acid effectually prevents the precipitation of any of the alkaloids.

[P1] **Syrupus Apomorphinæ (B.P.C.).**

**Dose.**— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Contains  $\frac{1}{16}$  gr. of apomorphine hydrochloride in 1 dr.

## ARGENTUM

Ag = 107.88.

**Argenti Acetas.**  $\text{CH}_3\text{COOAg} = 166.9$ .

In white crystals, **soluble** in water. A 1% solution is useful for the prevention and treatment of purulent ophthalmia in infants and causes less catarrh than the nitrate. Dilute salt solution may be used after it.

**Argenti Iodidum.** AgI = 234.8.

A light yellow powder, *insoluble* in water, alcohol and acids; soluble in solutions of potassium iodide, potassium cyanide and sodium thiosulphate.

**Storage.** In amber-coloured bottles protected from light.

**Uses.** In the freshly precipitated form this salt has been used in cases of ophthalmia. It has astringent properties. Efficacious in gonorrhœal ophthalmia. One drop of weak solution instilled 3 times a day or oftener in cases of extensive chemosis and danger of corneal sloughing.

Corneal opacities, conjunctivitis and pannus have been treated, commencing with 1% strength. In ulcer of the cornea it should be used cautiously.

A 5% silver iodide emulsion makes a good opaque medium for cystography, and has soothing antiseptic action on the bladder. Also of value for urethrogams.

**Nascent silver iodide** in 3% suspension may be produced from silver nitrate 2.2 g., potassium iodide 2.2 g., distilled water 50 ml., mucilage of Irish moss to 100 ml. For a light flocculent precipitate dissolve each in 50 ml. of water. To produce a coarse precipitate the salts are separately dissolved in 5 ml. of water, shaken and diluted with the mucilage. Gelatin 0.3% has also been used to dissolve the potassium iodide.

**Neo-Protosil** (*Parke, Davis, London*). A colloidal silver iodide compound prepared with a soluble protein base. Contains 20% of silver iodide. Used in solution for treatment of inflammations of the mucous membranes of the eye, nose, throat, etc.

**Argenti et Potassii Iodidum.** *Syn.* SILVER POTASSIUM IODIDE.  
KAgI<sub>2</sub> = 400.8.

The double iodide of potassium and silver. A crystalline substance readily soluble in water. Silver iodide is precipitated on dilution but precipitation is not complete until a fairly high dilution is reached.

**Preparation of an injection.** One part of crystallised silver potassium iodide and 4 parts of potassium iodide are dissolved in water, as required, in strengths of 0.5 g., 1 g. and 1.5 g., in 20 ml. in each case. Each of the dilutions contains a fine suspension of silver iodide and a solution of the double salt.

**GONORRHOEA.** The injection of 20 ml. into the meatus (apply tight bandage over glans for 15–30 minutes after injection), causes a rapid decrease of discharge after 6 injections and a complete disappearance of gonococci after 12 to 15 injections. Injections need only be given twice or thrice weekly, as silver iodide persists in the urethra.—S. R. Naidu, *Brit. med. J.*, i/1927, 139.

**Argenti Nitras** (*B.P., U.S.P. XI, Fr. Cx., P. Helv. V*).  
*Syn.* LUNAR CAUSTIC. AgNO<sub>3</sub> = 169.9.

**Dose.**— $\frac{1}{4}$  to  $\frac{1}{2}$  grain (0.008 to 0.016 g.) in a pill, best with kaolin ointment as an excipient. Up to  $\frac{1}{2}$  grain has been given. *U.S.P. XI* average dose  $\frac{1}{4}$  grain. *Fr. Cx.* max., single dose 0.03 g., max. in 24 hours 0.15 g.

A colourless, odourless, crystalline substance with a bitter, metallic taste.

**Soluble** 1 in 0.53 of water and 1 in 14 of alcohol 90%; slightly soluble in ether and glycerin.

**Incompatible** with organic material, e.g., rose water, if used instead of distilled water for preparing a lotion or pigment; also with tartaric acid, hydrocyanic acid, iodine and halides.

**Antidotes.** Empty stomach by stomach tube, using 2 oz. of

sodium chloride in 2 gallons of water, or give  $\frac{1}{2}$  oz. sodium chloride in 1 pint of water or milk, followed by an emetic. Demulcent drinks. Castor oil. Morphine,  $\frac{1}{4}$  gr. hypodermically for pain, if necessary.

**Silver nitrate stains** on the skin may be removed with mercuric chloride solution, or with potassium cyanide solution, or by wetting the skin and rubbing potassium iodide on the stain, leaving it on for a few hours.

In argyria a mixture of 1% of potassium ferricyanide and 6% of sodium thiosulphate injected intradermally removes a large part of the silver from the skin in old cases with deep pigmentation. A small dose of morphine and atropine cuts short sting of the injection.—A. W. Stillians and T. K. Lawless, *J. Amer. med. Ass.*, 1/1929, 21.

Occupational argyria in silver nitrate workers and silversmiths.—J. M. Harker and D. Hunter, *Brit. J. Dermat.*, 1935, 441.

**Uses.** Small doses internally check diarrhœa of children. In typhoid, where there is hæmorrhage,  $\frac{1}{8}$  grain every 3, 4 or 6 hours, or even as often as every 2 hours. Rectal injections are also useful for the bleeding of dysentery (60 grains in 3 pints). In laryngeal phthisis a spray  $\frac{1}{4}$  to 2 gr. to the ounce. In vomiting of pregnancy  $\frac{1}{8}$  grain in a wine-glass of water every 6 hours has been found effective. In gastric ulcer  $\frac{1}{8}$  grain in a pill 3 or 4 times daily half an hour before food useful. Solutions have also been used.

It is an excellent caustic for warts, condylomata, granulations, etc. In eczema of the flexures and particularly of mucous surfaces, a 2 to 3% solution, alternating with Lotio Calaminæ Oleosa, is valuable. Pigments, 1 to 5%, are used for the throat in pharyngitis and laryngitis, and applied to ulcers as a stimulant. Lotions for pruritus ani or vulvæ and eye-drops vary from 1 in 1000 to 1 in 100. 1% eye-drops are applied for the prophylaxis of ophthalmia neonatorum. Purulent ophthalmia and ulcerative blepharitis are treated with 1 to 2% drops. Ulcerative stomatitis is well treated by 0.5 to 2% solution. Glycerin 15% added to  $\frac{1}{2}$  to 2% silver nitrate solution renders it less painful, and possibly more effective.

Solutions of from 1 to 10%, either alone or in conjunction with tannic acid, may be employed in the treatment of burns (*see* Tannic Acid).

**URETHRAL AND VAGINAL INJECTIONS.** 0.02 to 0.2% (1 in 5000 to 1 in 500) is usually employed.

In lavage of the entire urethra in cystitis and for epithelial tumours of the urinary bladder 2 grains to the pint (1 in 5000 approx.) is sufficiently strong. In some cases it may be advisable to commence with a quarter of this strength. Hydrostatic pressure may be used, *i.e.*, the container being about 5 feet above the couch, instead of a syringe.

**URETHRAL BOUGIES** of silver nitrate contain  $\frac{1}{2}$  grain with theobroma basis. Give good results in obstinate cases of gonorrhœa.

**BURNS.** Spray or paint a 1% silver nitrate solution on burn and expose for 1 to 5 minutes to mercury vapour or tungsten arc lamp at 6 to 20 inches distance, or to real sunlight for  $\frac{1}{2}$  hour. No dressings used. Repeat if necessary in 24 to 36 hours.—*Brit. med. J.*, ii/1929, 668.

W. C. Wilson now uses a single application of a 10% solution of silver nitrate, preceded and followed by a 1% solution of gentian violet.—*Proc. R. Soc. Med.*, 1940, 34, 52.

For areas which cannot be constantly exposed to the air or cannot easily be kept dry the following jelly preparation is useful: Tragacanth 2, glycerol 10, powdered activated charcoal 15, silver nitrate 0.5, water to 100. This is preferable to tannic acid-acriflavine jelly.—W. C. Wilson, *Proc. R. Soc. Med.*, 1940, 34, 52.

**ERYSIPELAS** in the newborn treated with 4% solution, the lesion being swabbed 4-hourly day and night. The erysipelas tends to subside after 3 days' treatment, the average duration of which is 21 days. The treatment is almost painless.—H. Graner, per *Med. Annu.*, 1935, 135.

**PEMPHIGUS NEONATORUM.** Evacuation of the fluid by means of a pipette and the injection of 20% silver nitrate solution.—H. Carter and H. A. Osborn, *Brit. med. J.*, i/1936, 465.

**Gutt. Argent. Nitr.** (*N.I.F.*).

Silver nitrate  $\frac{1}{2}$  gr., distilled water to 2 dr. (approx. 0.5%).

**Liquor Argenti Nitratis** (*R.L.O.H.*). 4 or 8 gr. to 1 oz. of sterilised water (1 or 2% approx.).

As prophylactic, drops should not be used in stronger solution than 1%, and caution needed if used more than once or twice. Conjunctival hæmorrhage has followed 5 instillations of 1.5% solution.

**Pigmentum Argenti Nitratis Æthereum** (*L.H.*).

Silver nitrate 10 gr., water 1 dr., spirit of nitrous ether to 1 oz.

Caustic even when painted on a greasy skin. 3 to 10 grains to the ounce relieves pruritus ani and pruritus vulvæ. Useful in eczema and for prevention of bedsores.

**[D-P1-81] Pilula Argenti Nitratis et Morphine Acetatis.** *Syn.* CROCQ'S PILL. Contains  $\frac{1}{2}$  gr. of each salt, made with kaolin ointment.

**Unguentum Argenti Nitratis.** Silver nitrate 0.25 g., distilled water 25 g., lanoline 50 g., olive oil 25 g. For burns. Cleanse with sterile saline, removing blisters and apply spread on a soft cloth. Cover with oiled silk and bandage. It is painless and suitable for children.—M. Kissmeyer, *Bull. med.*, Paris, 1937, 51, 323; see also *Lancet*, ii/1936, 885.

**Unguentum Argenti Nitratis Compositum.** *Syn.* UNGUENTUM BILLROTHI (*P. Ned. V.*).

Silver nitrate 1, balsam of Peru 5, yellow soft paraffin 94.

**Natasil** (*Parke, Davis, London*). 1% silver nitrate solution. Supplied in wax capsules with paraffin lining, each containing 6 drops of the solution. For use in the prophylaxis of ophthalmia neonatorum.

**Partagon Bougies** (*Sandoz, London*). Bougies of silver nitrate associated with selected organic colloids. Supplied for men in two strengths: "mild" (0.75%  $\text{AgNO}_3$ ) and "strong" (2%  $\text{AgNO}_3$ ); and for women in one strength (1.5%  $\text{AgNO}_3$ ).

**Argenti Nitras Induratus** (*B.P.*). *Syn.* TOUGHENED CAUSTIC. Contains 5% of potassium nitrate moulded into caustic points. *U.S.P. XI* has 94.5%  $\text{AgNO}_3$ .

**Argenti Nitras Mitigatus** (*B.P.C.*, *P. Helv. V*, *P. Jap. V*). *Syn.* MITIGATED CAUSTIC, ARGENTI NITRAS DILUTUS.

Silver nitrate 1, potassium nitrate 2, fused together and moulded into sticks for use as caustic.

**Argenti Oxidum** (*B.P.C.*).  $\text{Ag}_2\text{O} = 231.8$ .

*Dose.*— $\frac{1}{2}$  to 2 grains (0.03 to 0.12 g.) in a pill with kaolin ointment.

Is not so caustic in action as silver nitrate. Continued administration may discolour the skin. It readily yields its oxygen, and will explode if mixed with such bodies as phenol and creosote. Soluble very slightly in water; insoluble in alcohol 90%. Has been given in epilepsy, chorea and dysentery. It stains the skin less than the nitrate.

**Novoxil Ointment** (*Squibb, New York; Savory & Moore, London*). Colloidal silver oxide ointment containing 5% anhydrous silver oxide, for use as a general antiseptic in the treatment of skin diseases, ulcerations and proctological conditions.

**Argenti Picras.**  $C_6H_2(OAg)(NO_2)_3 \cdot H_2O = 354.0$ .

*Syn.* SILVER TRINITROPHENOLATE, PICROTOLO.

Silver picrate is a yellow, crystalline substance which slowly discolours in light.

Sparingly **soluble** in water and alcohol; slightly soluble in acetone, chloroform, ether and glycerin.

**Uses.** Employed either in the form of a 1 or 2% solution, or as a compound powder (1% in purified kaolin) by insufflation, or as vaginal suppositories (2 gr. in a boroglyceride gelatin base), in the treatment of vaginitis due to *Trichomonas vaginalis* or *Monilia albicans*.

TRICHOMONAS VAGINITIS is successfully treated by one insufflation of 5 grains of silver picrate powder (30%) followed by daily dry swabbing and the insertion of a pessary containing 2 grains of silver picrate. The pessary treatment is continued for 6 days and is then followed by another insufflation. No douching is allowed during the treatment and no treatment is given during the menstrual period. After insufflation the *Trichomonas vaginalis* disappeared on the next day in 26 out of 28 cases.—W. M. Mascal, *Brit. med. J.*, i/1937, 1115.

**Argentoproteinum** (*B.P. Add. I*). *Syn. and Prop. Names.* ARGENTI PROTEINAS (*B.P.C.*), ARGENTUM PROTEINICUM (*Fr. Cx.*, *P. Ital. V*, *P. Jap. V*, *P. Ned. V*, *F.E. VIII*, *P. Belg. IV*, *P. Helv. V*), ARGENTUM PROTEINICUM FORTE (*U.S.P. XI*), STRONG SILVER PROTEIN, SILVER PROTEIN, ARGEIN (*Allen & Hanburys, London*), PROTARGOL (*Bayer Products, London*).

**Dose.**—1 to 3 grains (0.06 to 0.2 g.). No dose is given in *B.P. Add. I*.

**Note.**—The *U.S.P. XI* names, Strong Silver Protein for preparations containing 8% of Ag and Mild Silver Protein for those containing 20% or more of Ag, are based on the fact that the former are the more strongly bactericidal. They are also more irritant.

A fine, brownish-yellow, somewhat hygroscopic powder containing 7.5 to 8.5% of Ag. *P. Svec.* has 7.8 to 10% of Ag.

**Soluble** about 1 in 2 of water; almost insoluble in alcohol, chloroform and ether. Aqueous solutions may be prepared by shaking on to surface of cold water and allowing to dissolve slowly, or by triturating to a cream with water and diluting as required.

**Incompatibility with Alkaloids.** Solutions of many silver-protein compounds are alkaline and precipitate alkaloids from solutions of their salts. Where the combination of silver-protein compound and cocaine is necessary, cocaine nitrate should be prescribed.

**Uses.** Strong silver protein has a more prolonged but much less powerful antiseptic action than silver nitrate, and has the advantages of being non-corrosive and unaffected by body secretions. It is especially useful for application to the mucous membrane and is employed as an antiseptic in stomatitis, tonsillitis, conjunctivitis and ophthalmia neonatorum in 0.5 to 10% solutions: For the urethra, 1 to 2% solutions are used, or in chronic gonorrhœa up to 10%. As a urethral irrigation a 0.1% solution is employed. Pessaries and bougies for use in gonorrhœa are made with 5 to 10%. A 0.5% agar jelly containing 0.5% of silver protein (Schindler's jelly) has also been applied to the urethra.



in gonorrhœa. As enemata in dysentery and colitis solutions of 0.1 to 1% are suitable.

For the early preventive treatment of venereal disease the parts are thoroughly washed with soap and water and a 2% solution of strong silver protein solution is then injected into the urethra and retained for 5 minutes. The glans is then inuncted with 30% mild mercurous chloride ointment for 5 minutes. This has a marked efficacy if employed within an hour of exposure and is fairly effective up to 3 hours.

Solutions should be freshly prepared since old solutions may be slightly caustic.

Argyria can result from the use of silver-containing intranasal medication. A 100% increase in such cases reported during a recent period of 5 years. In addition, rabbits treated intranasally with 5% mild protein silver, showed lung changes. There is a clear case against the intranasal use of silver preparations.—B. L. Bryant, per *J. Amer. med. Ass.*, 1/1940, 1017.

**Guttæ Argenti Proteinatis (R.L.O.H.).** Silver protein 8, 20, 40 or 60 gr., sterilised water to 1 oz. *N.I.F.* has 40 gr. in 1 oz.

**Neisser's Bougies.** Silver proteinate 1%, phenazone 2%, in oil of theobroma or in gelatin basis. For the treatment of gonorrhœa.

**Hegonon (Schering, London).** Ammoniacal silver nitrate derivative of albumose containing 7% Ag. Tablets containing 3.75 gr. for local treatment of gonorrhœa in  $\frac{1}{2}$  to  $\frac{1}{4}$  solution.

### **Argenti Proteinæ Mite (B.P.C.).**

**Syn. and Prop. Names.** ARGENTO-PROTEINUM MITE, ARGENTI NUCLEINAS, ARGENTI VITELLIN, ARGENTUM VITELLINATUM (*Fr. Cx., P. Belg. IV*), PLATA VITELINA (*F.E. VIII*), ARGENTUM PROTEINICUM MITE (*U.S.P. XI*), MILD PROTARGIN, ARGYROL (*Barnes, Philadelphia; Fassett & Johnson, London*) (20% Ag, also in solution-tablets containing 0.5 g.), ARVITIN (*Johnson & Sons, London*) (20% Ag, with egg yolk protein), CARGENTOS (*Sharp & Dohme, London*) (20 to 25% Ag, with casein), LUNARGEN (*Lilly, London*) (20% Ag).

**Note.**—The name Mild Silver Protein is given to this group of compounds because, although containing more silver than the strong silver protein compounds, they are less bactericidal, and also less irritant.

A brown powder or nearly black scales or granules containing 19 to 25% of Ag.

**Soluble** slowly but readily in water, almost insoluble in alcohol, chloroform and ether.

**Incompatible** with cocaine hydrochloride, but compatible with 1% atropine sulphate.

**Uses.** Is used for the same purposes as silver protein but in stronger solutions, especially where irritation must be avoided. For corneal ulcers and as a spray for the nose and throat may be used up to 50% strength.

In purulent conjunctivitis (gonorrhœal, neonatorum, etc.), free instillation of 25% solution every 3 or 4 hours; catarrhal conjunctivitis, 5 to 20% 1 or more times daily; trachoma, 25% solution rubbed with force on wool into lids once daily; dacryocystitis, 25% solution. For gonorrhœa may be used in various strengths

up to 20%. As a rectal or urethral irrigation solutions of 0.1 to 1% are employed. Pessaries for vaginitis may contain 5 to 10%.

Ulcerative colitis has been treated by washing out with 1½ pints of 1% solution at 80°F.

**Gutt. Argent. Vitellin.** (N.I.F.). Mild silver protein 40 gr., distilled water to 1 oz.

[P1] **Guttæ Argyrolis cum Adrenalina** (Mid. H.).

Argyrol 25 gr., solution of adrenaline hydrochloride 20 m., glycerin 15 m., water to 1 oz. Three drops into each nostril night and morning in acute or chronic sinusitis.

**Unguentum Argenti Proteinatis Mitis** 2% with paraffin basis in eczema-tous conjunctivitis and keratitis.

**Silver Gelatose.** *P.G. VI* (15% Ag), *P. Svec. X* (16%).  
*Prop. Name.* ALBARGIN (*Bayer Products, London*).

According to the patent specification, gelatose (produced by hydrolysis of glutin, etc., by acid or alkali) 10 g., is dissolved in water 10 ml. and mixed, after neutralising, with silver nitrate 1.5 g. in water 5 ml. The mixture is evaporated to dryness *in vacuo*. The salt thus obtained is a yellow-white powder of sand-like appearance containing 15% of silver.

**Soluble** about 1 in 2 of water, and about 1 in 130 of alcohol 90%. For gonorrhœa a 0.2% solution injected 4 or 5 times daily, or irrigation with 1 to 4000 solution. 0.5 to 3% for ophthalmic use. In bacillary dysentery silver gelatose by rectal injection is of great value—not in amœbic cases.

**Incompatible** with chlorides and tannin.

**Stains on fabric** may be removed with hot sodium thiosulphate solution 1 in 10.

**Silver Gelatose Enema.**

*Dose.*—1 pint increased to 1½ pints of strength 1 gr. per oz. on successive days.

**Protosil** (*Parke, Davis, London*). A combination of colloidal silver with an albuminoid. Contains about 20% of silver. Used in solution for treatment of inflammatory conditions of the mucous membranes.

**Argentum Colloidale** (*P. Helv. V, P.G. VI, Fr. Cx., P. Ned. V, P. Svec. X, P. Jap. V*). *Syn.* ARGENTUM CRÉDÉ, PLATA COLOIDAL (*F.E. VIII*).

A preparation of silver in combination with protein, containing at least 70% of Ag (*P. Ned. V* 74.5 to 80%, *P. Svec.* 72 to 80%). In green or bluish-black plates with metallic lustre and bitter metallic taste.

**Soluble** slowly 1 in 2.5 of water; insoluble in organic solvents. Aqueous solutions should be freshly made as required and filtered.

**Incompatible** with dilute mineral acids and concentrated salt solutions. In the latter case the precipitate dissolves on diluting with water.

**Uses.** For local treatment in the form of solution or ointment, 1 to 15%. For ophthalmic use 1 to 10% solutions are employed. Diphtheritic membrane is said to disappear under swabbing with 5% solution. Intravenously, 2 to 10 ml. of ½ to 2% solution for septic affections such as endocarditis. Orally as a ½ to 1% solution or in pills for gastric and intestinal catarrh.

**Pommade à l'Argent Colloidal** (*Fr. Cx.*). Colloidal silver 15 g., water 15 g., wool fat 35 g., Vaseline 35 g. Make a paste of the colloidal silver and water; melt the wool fat and Vaseline, cool, and incorporate the paste in the base.

**Unguentum Crêdê.** Collargol 15, white wax 10, benzoinated lard 75. For eczema, syphilis and gonorrhœa, and as a prophylactic to gonorrhœal ophthalmia.

**Unguentum Argenti Colloidalis** (*P. Jap. V*). Colloidal silver 10%, in equal parts of wool fat and Vaseline.

**Argental** (*Abbott Laboratories, London*). A mild colloidal silver preparation containing 16% silver bromide. It may be used dissolved in water, in strengths varying from 5 to 40% in the treatment of infections of the eye, nose, throat and urinary tract.

**Cryptargol** (*Anglo-French Drug Co., London*). A silver derivative of thio-glycerin sulphonate of sodium, containing 35% of Ag. Supplied in pills or syrup for internal use as a gastro-intestinal antiseptic, and as a concentrated (10%) solution for external use as a general antiseptic and for use in dermatology, urology and gynaecology. Also as ovules (in vaginitis, metritis, etc.) and as collyria (1% and 5%).

**Neo-Reargon** (*Napp, London*). Compound of silver and anthraquinone glycosides containing about 14% of Ag. For urethral injection in gonorrhœa in 1·5 to 2·5% solution, and for vaginal irrigation in 1 to 2% solution.

## ARSENUM

As=74·91

[P1] "*Arsenical substances, the following, except those specified in Part II of this List:—Arsenic, halides of; oxides of arsenic; arsenates; arsenites; organic compounds of arsenic.*"

[P2] "*Arsenical substances, the following:—Arsenic sulphides; arsenious oxide; calcium arsenates; calcium arsenites; copper acetarsenites; copper arsenates; copper arsenites; lead arsenates; potassium arsenites; sodium arsenates; sodium arsenites; sodium thioarsenates.*"

[81] "*Arsenical poisons except substances containing less than the equivalent of 0·01% of arsenic trioxide and except dentifrices containing less than 0·5% of acetarsol.*"

[83] "*Arsenical poisons—in pyrites ores or sulphuric acid containing arsenical poisons as natural impurities.*"

[86] "*Arsenical poisons—specify proportion as the proportion of arsenic trioxide ( $As_2O_3$ ) or arsenic pentoxide ( $As_2O_5$ ) that the preparation would be calculated to contain on the assumption that the arsenic (As) in the poison had been wholly converted into arsenic trioxide or arsenic pentoxide as the case may be.*"

[P2-81] **Arseni Trioxidum** (*B.P., U.S.P. XI, P. Dan.*). *Syn.* ACIDUM ARSENIOSUM, ARSENIC, WHITE ARSENIC, ARSENIOS ANHYDRIDE (*Fr. Cx.*), ARSENIOS ACID, ARSENIOS OXIDE, ACIDUM ARSENICOSUM (*P. Helv. V, P. Jap. V*).  $As_2O_3 = 197·86$ .

*Dose.*— $\frac{1}{10}$  to  $\frac{1}{12}$  grain (0·001 to 0·005 g.). *U.S.P. XI* average dose  $\frac{1}{10}$  grain.

Maximum single dose  $\frac{1}{12}$  grain (0·005 g.); maximum daily dose  $\frac{1}{4}$  grain (0·016 g.). Possible fatal dose 2 grains.

Made by roasting arsenical ores. It occurs in white lumps or powder, and is usually a mixture of two varieties, one of which is opaque and crystalline and the other transparent and vitreous. The latter slowly changes to the former.

**Soluble** very slowly about 1 in 65 of water (*B.P.*). The solubility varies with the relative proportion of the two varieties present, the vitreous being more readily soluble than the crystalline. With some samples the solubility is not more than about 1 in 100. More soluble in water acidified with hydrochloric acid and in alkaline hydroxide and carbonate solutions. Soluble about 1 in 8 of glycerin; slightly soluble in alcohol 90% and ether.

**Incompatible** with iodine, iron salts, lime water, magnesia and tannins.

**Antidotes.** Empty stomach by emetic, or by stomach tube, using 2 gallons of water to which has been added precipitated ferric hydroxide (2 oz. of solution of ferric chloride, add sodium carbonate till effervescence ceases, filter and use precipitate). Give 4 oz. of arsenic antidote *B.P.C.*, repeating the dose if necessary. (If this is not available, give 1 oz. of tincture of ferric chloride in 4 oz. of water with 1 oz. of sodium bicarbonate added; or give magnesia mixed with water freely.) Keep patient warm. Give castor oil or saline purgative (magnesium sulphate). Demulcent drinks freely. Stimulants, *e.g.*, caffeine sodium benzoate, 2 gr. hypodermically, may be necessary for collapse, or morphine,  $\frac{1}{4}$  gr. hypodermically, for pain. Saline infusion if required.

For use of sodium thiosulphate and sodium hydrosulphite in arsenical poisoning, see p. 110.

**Antidotum Arsenum** (*B.P.C.*, *P. Helv. V*, *P. Dan.*). *Syn.* FERRI HYDROXIDUM CUM MAGNESII OXIDO. *F.E. VIII* and *P. Jap.* use ferric sulphate, and in other pharmacopœias:

**Dose.**—4 ounces (120 ml.).

Contains freshly precipitated ferric hydroxide and light magnesium oxide.

Two solutions are stored ready for use:—(1) Strong solution of ferric chloride 288 m. mixed with  $2\frac{1}{2}$  oz. of water. (2) Light magnesium oxide  $87\frac{1}{2}$  gr., triturated to a smooth paste with water and diluted to 15 oz. For use add  $3\frac{3}{4}$  oz. of the magnesium oxide suspension, well shaken, to 400 m. of the ferric chloride solution.

**Magma Ferri Hydroxidi** (*U.S.P. XI*).

**Average dose.**—4 ounces (120 ml.).

Arsenic antidote kept ready for use in two parts: (1) 40 ml. of solution of ferric sulphate diluted to 125 ml., (2) 10 g. of magnesium oxide or 300 ml. of Magma Magnesiae diluted to about 750 ml. in a 1000 ml. bottle. The two are mixed for use.

**Acute arsenical poisoning.** Overdosage with arsenic is indicated by vomiting and diarrhoea, numbness and tingling in the feet, followed by muscular cramps, suppression of urine, intense thirst, prostration and collapse. In criminal cases of arsenical poisoning the symptoms may be those of acute arsenical poisoning, such as one would expect from a single dose, masked by those of prolonged action of arsenic. Thus, symptoms of arsenical neuritis or renal or liver disease may be superimposed upon those of the acute gastrointestinal symptoms. Arsenic can be found months or years after taking, in the nails and hair.

**Chronic arsenical poisoning** is characterised by a disposition to œdema, especially of the face and eyelids, a feeling of stiffness in those parts, pruritus, tenderness of the mouth, loss of appetite, nausea, sickness, and diarrhoea. Continued use of small doses over long periods may cause dryness of the skin, pigmentation and keratinisation, which may be accompanied by peripheral neuritis.

**Uses.** Arsenic is given internally after meals as a general tonic and it is one of the few substances which really deserves this name, since it increases both the weight and strength of the patient, *e.g.*, in wasting diseases such as tuberculosis and certain types of neurasthenia with malnutrition. It was at one time much employed in chorea, beginning with small doses rapidly increased to the limit of tolerance. In the treatment of the secondary anæmias, though possessing no apparent beneficial action by itself, it increases the hæmatinic effects of iron. In leukæmia it often produces marked temporary improvement; commencing with 3 to 5 m. of Fowler's solution three times daily, the dose is gradually increased to the limit of tolerance and then reduced to a maintenance level of 5 m. thrice daily, continued for 3 or 4 months. Fowler's solution, 2 dr. to the ounce of water, is a valuable local application in Vincent's angina.

Externally it has a caustic action, and is put into the cavities of carious teeth to kill the nerves (*see* Pasta Arsenicalis).

**ECZEMA.** Arsenic continues to hold an important place in the therapy of chronic eczema. It should never be used during the acute phase. In the subacute stage it should be given only if the eruption proves refractory to other therapeutic measures. Solution of potassium arsenite is prescribed in gradually ascending doses, starting with 3 m. twice daily after meals and increasing the dose by 1 m. daily until 20 m. is taken; this dose can be maintained for several weeks, a course of treatment usually lasting from four to six weeks. Arsenical medication must not be frequently repeated and the danger of delayed late effects must be kept in mind. At the first signs of intolerance, *e.g.*, sweating of the palms, coated tongue, dryness of the throat, abdominal pain, and puffiness of the eyelids it should be discontinued.—F. Wise and J. Wolf, *J. Amer. med. Ass.*, ii/1938, 2106.

**HODGKIN'S DISEASE.** A severe case of Hodgkin's disease in a young man of 28 successfully treated with colloidal elemental arsenic. Treatment was begun in September 1935 with daily intravenous doses of 0.25 ml. gradually increased to 2 ml., and gradually changed from 2 ml. daily to 3 ml. three times a week and finally to 5 ml. tri-weekly. In March, 1937, the patient was looking and feeling well and all the enlarged glands had disappeared.—A. C. Hendrick and E. F. Burton, *Canad. med. Ass. J.*, i/1937, 519.

[D-P1-S1] **Gossypium Arsenii (R.D.H.).** ARSENIUS WOOL.

Arsenic trioxide 5 parts, tannic acid 2 parts, morphine acetate 10 parts, liquefied phenol sufficient to make a thin paste. Mix with a sufficiency of finely cut cotton wool. Used in the same way as Pasta Arsenicalis. Some formulæ contain creosote instead of phenol.

[P1-S1] **Granula Acidi Arsenicosi (Fr. Cx., P. Dan.).** *Syn.* GRANULA DIOSCORIDIS.

Contains 1 mg. of arsenic trioxide. *Dose.*—1 to 5.

[P2-S1] **Liquor Arseni Acidus (B.P.C.).** *Syn.* LIQUOR ARSENICI HYDROCHLORICUS.

*Dose.*—2 to 8 minims (0.12 to 0.5 ml.). Contains 1% of arsenic trioxide in hydrochloric acid and water. Is compatible with acid mixtures.

[P2-S1] **Liquor Acidi Arsenosi (U.S.P. XI).**

*Average dose.*—3 minims (0.2 ml.).

Contains 1% of arsenic trioxide and 5% of dilute hydrochloric acid; it resembles Liquor Arseni Acidus, B.P.C.

**[P1-81] Liquor Arseni Alkalinus (B.P.C.).**

*Dose.*—2 to 8 minims (0·12 to 0·5 ml.).

Contains 1% of arsenic trioxide, dissolved with the aid of potassium carbonate and coloured with compound tincture of lavender.

**Incompatible** with Liquor Strychninæ Hydrochloridi. Employ Liquor Arsenicalis. Poisoning has occurred.

**[P2-81] Liquor Arsenicalis (B.P.). Syn. FOWLER'S SOLUTION.**

*Dose.*—2 to 8 minims (0·12 to 0·5 ml.).

Contains the equivalent of 1% of arsenic trioxide in neutral solution. The oxide is dissolved in potassium hydroxide and neutralised with dilute hydrochloric acid. The solution contains no compound tincture of lavender (*see* Liquor Arseni Alkalinus), but the addition of 0·5% of spirit of lavender to prevent growth of moulds has been recommended.

Numerous complaints have been made that this preparation is liable to yield a deposit of  $As_2O_3$  crystals and to become fungoid. After thorough investigation E. M. Smelt (*Quart. J. Pharm.*, 1933, 375) reported that the growth of moulds could be inhibited by adjusting the pH to 2·0 or to 8·0, and the deposition of crystals by adjusting the pH to less than 3·0 or more than 9·0. The paper gives references to the principal previous investigations.

VINCENT'S ANGINA. Arsenic is specific; full doses of the Liquor Arsenicalis may be given three-hourly, or it may be used as a paint with glycerin.—E. Watson-Williams, *Practitioner*, i/1936, 47. *See also* Pigmentum Ipecacuanhæ et Arsenici, p. 657.

**[P2-81] Liquor Potassii Arsenitis (U.S.P. XI).**

*Average dose.*—3 minims (0·2 ml.).

The same strength as Liquor Arsenicalis, B.P., but prepared with potassium bicarbonate and alcohol instead of potassium hydroxide and hydrochloric acid, and therefore alkaline in reaction. Resembles Liquor Arseni Alkalinus (B.P.C.) but is colourless.

**[P2-81] Liquor Arsenicalis Glycerinatus (A.P.F.).**

Heat arsenic trioxide 87½ gr. with glycerin 2 oz. to 150° to dissolve. Cool, add water 17 oz., then compound tincture of lavender 288 m. and water to 1 pint.

Solutions of arsenic trioxide in dilute glycerin are liable to give a very slight deposit of a crystalline form of  $As_2O_3$  on standing for 2 to 3 months.

**[P2-81] Soluté d'Arsenite de Potassium (Fr. Cx.). Syn. FOWLER'S SOLUTION (Fr. Cx.).**

*Dose.*—Max. single 0·5 g., max. in 24 hours 1 g.

Dissolve arsenic trioxide 1 g., and potassium carbonate 1 g., in 2 g. of water. Add 40 g. of water, 12 g. of alcohol 90%, 3 g. of "Alcoolat de Melisse Composé" and sufficient water to produce 100 g. Other foreign pharmacopœias have similar preparations.

**[P2] Mistura Antimalarica (Bacelli) (P. Ital. V). Dose.**—½ to 1 ounce (15 to 30 ml.).

Quinine sulphate 3 g., iron and potassium tartrate 7·5 g., distilled water 300 g., Fowler's solution 25 drops.

**[P2] Mistura Arseni Quininae et Ferri. Syn. BACCELLI'S MIXTURE (slightly modified).**

*Dose.*—½ to 1 ounce (15 to 30 ml.).

Dissolve quinine sulphate 3 in water 150 with aid of a little dilute sulphuric acid. Then dissolve green ammonio-citrate of iron 5 in water 150, mix and add Fowler's solution 3. Employed in malaria.

**[P1-81] Pasta Arsenicalis (B.P.C.).**

Arsenic trioxide 2 and morphine hydrochloride 1, mixed to a paste with creosote (*exempt* [D]). R.D.H. is similar but uses morphine acetate.

The equivalent of about ⅛ grain of arsenic trioxide is sufficient.

Apply as follows:—Remove as much carious tissue as possible, exclude moisture and disinfect. Apply the paste as near pulp as possible and protect by concave cap. Seal cavity carefully with mastiche in chloroform.

For preparations of similar composition also *exempt* [D] see pp. 1140, 1141.

[P2-S1] **Caustiscin** (*Saccharin Corporation, London*). Pellets containing arsenious oxide and procaine hydrochloride for devitalising dental pulp. Prepared in three different strengths:—"Blue," contains 40%  $\text{As}_2\text{O}_3$ —has powerful action and should be left for 24 hours only; "Yellow," contains 30% of  $\text{As}_2\text{O}_3$ —slower in action and may be left for 3 to 5 days; "Black," contains slow and mildly acting metallic arsenic (40% As), used particularly for milk teeth.

[P2-S1] **Pilula Acidi Arseniosi et Ferri Redacti**.—MONCKTON.

*Dose*.—1 to 3 grains. Arsenic trioxide 12 gr., reduced iron 1 oz., excipient *q.s.*

[P1-S1] **Pilula Arsenicalis et Strychninae** contains  $\frac{1}{80}$  grain (0.0013 g.) of each.

[P2-S1] **Pilulae Asiaticae** (*B.P.C.*). *Dose*.—1 or 2 daily.

Each pill contains arsenic trioxide  $\frac{1}{12}$  gr. (0.005 g.) and black pepper  $\frac{1}{2}$  gr. (0.05 g.). In chronic skin affections.

In psoriasis this is a convenient method of giving arsenic.

*P.G. VI* contains  $\frac{1}{80}$  gr. (0.001 g.) of arsenic trioxide, and  $\frac{1}{2}$  gr. (0.03 g.) of pepper.

[P2-S1] **Tablets of Arsenic, Iron and Quinine** contain arsenic trioxide  $\frac{1}{80}$  gr., ferric hypophosphite 2 gr., quinine acid sulphate 1 gr.

[P2-S1] **Tablets of Arsenious Acid and Mercuric Chloride**  $\frac{1}{80}$  gr. (0.001 g.) of each. In exophthalmic goitre have been given thrice daily.

[P1-S1] **Liquor Potassii Arsenatis et Bromidi** (*B.P.C.*).

*Syn.* CLEMENS' SOLUTION, LIQUOR ARSENII BROMIDI.

*Dose*.—2 to 8 minims (0.12 to 0.5 ml.), once or twice a day.

A solution containing potassium arsenate and potassium bromide equivalent to 1% *w/v* of  $\text{As}_2\text{O}_3$  and 0.5% *v/v* of bromine.

The solution has been employed in epilepsy and diabetes.

[P1-S1] **Arseni Triiodidum** (*B.P., U.S.P. XI, Fr. Cx.*).

*Syn.* ARSENII IODIDUM, ARSENIOUS IODIDE.  $\text{AsI}_3 = 455.7$ .

*Dose*.— $\frac{1}{16}$  to  $\frac{1}{2}$  grain (0.004 to 0.016 g.), in a pill. *U.S.P. XI* average dose  $\frac{1}{12}$  grain.

The two elements combine, forming orange-coloured crystals. It should be recrystallised so as to exclude a melted mixture of elementary arsenic and iodine, or powdered arsenic 10, may be mixed with iodine 51 in presence of water, digested at gentle heat and evaporated to dryness.

**Soluble** 1 in 11 of water, forming a slightly cloudy acid solution, 1 in 40 of alcohol 90%, 1 in 18 of carbon disulphide, 1 in 73 of benzene; slightly soluble in ether, chloroform and carbon tetrachloride.

Solution 1% in 1 to 10 drop doses in milk, useful for lymphatic and scrofulous children, has marked iodine effect. Also used externally in the treatment of lupus and other skin conditions requiring a powerful stimulant.

It is of use in diseases of the alimentary canal, especially gastritis, and in all cases of neuritis.

**[P1-81] Injectio Arseni Iodidi.**

*Dose.*— $\frac{1}{100}$  grain (0.0006 g.) in 6 minims (0.4 ml.) of sterile water. The strength may be increased if desired.

**[P1-81] Liquor Arseni et Hydrargyri Iodidi (B.P., Fr. Cx.).**

*Syn.* DONOVAN'S SOLUTION.

*Dose.*—5 to 15 minims (0.3 to 1 ml.).

Contains arsenic triiodide and mercuric iodide, of each 1%.

Given for syphilitic skin diseases.

**Incompatible** with potassium iodide and sal volatile (cf. Nessler's reagent), also with alkaloids and acids.

Should be *freshly prepared* or stored in small bottles completely filled. A sample after 14 months was found to contain no arsenous arsenic.—T. Tusting Cocking, *Quart. J. Pharm.*, 1929, 409.

**DISSEMINATED SCLEROSIS.** Most neurologists consider arsenic the most useful drug. 10 to 12 m. of Donovan's solution in  $\frac{1}{2}$  oz. of water may be taken regularly thrice daily for months. Tincture of belladonna 10 m. may be added if there is faulty control of the bladder.—Macdonald Critchley, *Med. Fr.*, i/1936, 520.

**[P2-81] Cupri Arseni.** *Syn.* SCHEEL'S GREEN.  $\text{Cu}_3\text{As}_2\text{O}_6 = 436.6$ .

*Dose.*— $\frac{1}{100}$  to  $\frac{1}{25}$  grain (0.0006 to 0.0025 g.).

Amorphous green powder, used in various intestinal affections, cholera morbus, cholera infantum, diarrhoea, dysentery and typhoid. *Dose* for adults  $\frac{1}{100}$  to  $\frac{1}{25}$  grain every 10 minutes for an hour, then hourly; for children, half this quantity. Small repeated doses essential. For chlorosis and functional anaemia  $\frac{1}{50}$  to  $\frac{1}{25}$  grain thrice daily are given.

**[P1-81] Acidum Arsenicum (B.P.C.)** *Syn.* ORTHO-ARSENIC ACID.

$\text{H}_3\text{AsO}_4 \cdot \frac{1}{2}\text{H}_2\text{O} = 151.0$ .

*Dose.*— $\frac{1}{50}$  to  $\frac{1}{25}$  grain (0.001 to 0.005 g.).

A crystalline powder soluble about 2 in 1 of water, and very soluble in alcohol 90%. Arsenates are said to be twice as active as arsenates.

**[P1-81] Ferri Arsenas (B.P.C., Fr. Cx., F.E. VIII).**

*Dose.*— $\frac{1}{15}$  to  $\frac{1}{2}$  grain (0.004 to 0.016 g.). *Fr. Cx.* has *max. single dose*  $\frac{1}{2}$  grain, *max. in 24 hours*  $2\frac{1}{2}$  grains; *F.E. VIII* gives  $\frac{1}{15}$  grain and  $\frac{1}{2}$  grain respectively.

This is an amorphous greenish powder and consists of ferrous and ferric arsenates and iron oxide, the ferrous iron content being equivalent to not less than 10% of  $\text{Fe}_3(\text{AsO}_4)_2$ . The ferrous arsenate rapidly oxidises in the air. In chronic skin affections of all kinds.

**[P2-81] Sodii Arsenas Anhydrosus (B.P.C.).** *Syn.* SODIUM ARSENATE, DISODIUM HYDROGEN ARSENATE.  $\text{Na}_2\text{HAsO}_4 = 185.9$ .

*Dose.*— $\frac{1}{15}$  to  $\frac{1}{10}$  grain (0.0015 to 0.006 g.).

Sodium arsenate crystallises with 7 or with 12 molecules of water. The former,  $\text{Na}_2\text{HAsO}_4 \cdot 7\text{H}_2\text{O} = 312.0$ , is included in *I.A.*, *Fr. Cx.*, *P. Ned. V.*, *P. Helv. V.*, *P. Belg. IV.*, *P. Ital. V.*, and *P. Dan.* *Fr. Cx.* has *max. single dose*  $\frac{1}{8}$  grain; *max. during 24 hours*,  $\frac{1}{2}$  grain approximately.

The anhydrous salt, in white powder, dried at  $150^\circ$ , contains 61.8% of  $\text{As}_2\text{O}_5$ . 1 of the anhydrous salt equals 1.68 of the salt with  $7\text{H}_2\text{O}$ .

**Soluble** 1 in 6 of water. Slightly soluble in alcohol.

Possesses the therapeutic properties of arsenic and is used similarly. It is stated to have been found beneficial in deafness;



$\frac{1}{3}$  grain (in pill) followed by  $\frac{1}{4}$  grain the next day—altogether, 40 to 60 pills in as many days.

**[P1-81] Injectio Sodii Arsenatis et Strychninae.**

*Dose.*—5 to 10 minims (0.3 to 0.6 ml.) hypodermically.

Sodium arsenate 2 ( $\frac{1}{30}$  gr. in 10 m.), strychnine hydrochloride 1 ( $\frac{1}{30}$  gr. in 10 m.), water to 600.

**[P1-81] Injectio Sodii Arsenatis et Strychninae et Quininae** contains 1 gr. of quinine acid hydrochloride added to 10 m. of the above.

**[P2-81] Liquor Sodii Arsenatis (B.P.C.).**

*Dose.*—2 to 8 minims (0.12 to 0.5 ml.). 1% of the anhydrous salt.

**[P2-81] Pearson's solution of arsenic** used on the Continent, *e.g.*, *P. Ital. V*, is 1 of crystallised sodium arsenate ( $7H_2O$ ) in water 600; *P. Belg. IV* is 1 in 1000.

## ORGANIC ARSENIC COMPOUNDS

An organic arsenic compound, as distinct from the inorganic form, has the arsenic in combination with a carbon atom. This appears to lessen its toxic properties. Furthermore, arsenum acts either as a tri- or penta-valent element and, broadly, the former compounds are more potent upon protozoa. Examples of the first class are arsphenamine and of the second, sodium cacodylate, sodium arsanilate, tryparsamide, etc. The compounds are classified below under the headings (i) *Aliphatic*, (ii) *Aromatic*, (iii) *Bis-phenyl nucleus* bodies, as far as practicable.

### (I) Aliphatic Series.

**[P1-81] Acidum Cacodylicum (B.P.C.).**

*Syn.* DIMETHYLARSONIC ACID.  $(CH_3)_2AsO \cdot OH = 138.0$ .

*Dose.*— $\frac{1}{2}$  to 2 grains (0.03 to 0.12 g.).

The ultimate product of oxidation of cacodyl, tetramethylarsine,  $(CH_3)_2As-(CH_3)_2$ , discovered by Bunsen in 1842, and of cacodyl oxide, *syn.* alkarsin,  $(CH_3)_4As_2O = 226.0$ . Colourless hygroscopic crystals neutral to methyl orange, acid to phenolphthalein.

*Soluble* about 2 in 1 of water, 1 in 4 of alcohol 90%, readily in chloroform.

Although containing 54.3% of As, equivalent to 71.6% of  $As_2O_3$ , it is relatively non-toxic—similarly with the salts. It will be noted that this acid has only 1 OH group, hence it is not so toxic as its parent arsonic acid, with 3 OH.

**[P1-81] Calcii Cacodylas.**  $[(CH_3)_2AsO_2]_2Ca = 314.0$ .

*Dose.*— $\frac{1}{2}$  to 2 grains (0.03 to 0.12 g.) *per os* or intramuscularly.

A white amorphous powder. Soluble 2 in 1 of water, 1 in 2 of alcohol. Its uses are the same as those for sodium cacodylate, *q.v.*

**[P1-81] Ferri Cacodylas.**  $[(CH_3)_2AsO_2]_2Fe = 466.8$ .

*Dose.*— $\frac{1}{2}$  to  $\frac{1}{4}$  grain (0.016 to 0.03 g.) *per os* three times daily, up to 5 grains *per diem* may be given. Intramuscularly  $\frac{1}{2}$  to 1  $\frac{1}{2}$  grains (0.03 to 0.1 g.) *per diem*. Intravenously 1 grain (0.06 g.) in 5 ml.

Yellowish powder soluble 1 in 15 of water. Used for anaemia and chlorosis, also in glandular swellings, *e.g.*, in syphilis, hypodermically.

**[P1-81] Ferosin (Richter, London).** Ampoules contain iron cacodylate  $\frac{1}{2}$  gr., strychnine nitrate  $\frac{1}{30}$  gr., sodium glycerophosphate  $1\frac{1}{2}$  gr. in 1 ml. *Dose.*—Three subcutaneous injections of 1 ml. weekly. Tablets contain strychnine nitrate  $\frac{1}{30}$  gr., iron cacodylate  $\frac{1}{30}$  gr., calcium glycerophosphate  $2\frac{1}{2}$  gr. *Dose.*—1 or 2 tablets daily. Asthenic conditions and anaemia.

[P1-S1] **F.N.S. (Ferruginous Neurasthenic Serum)** (Allen & Hanburys, London). Ampoules contain iron cacodylate 0.01 g., sodium glycerophosphate 0.1 g., strychnine cacodylate 0.0005 g., in normal saline, to 1 ml. *Dose*.—1 ml. intramuscularly for 12 days. Anæmia and debility.

[P1-S1] **Ferruginous Ampoules** (Wilcox, JozEAU, London) contain iron cacodylate 0.01 g. ( $\frac{1}{10}$  grain), sodium glycerophosphate 0.1 g. ( $\frac{1}{10}$  grains) and strychnine cacodylate 0.0005 g. ( $\frac{1}{200}$  grain) in 1 ml. *Dose*.—1 ml. subcutaneously or intramuscularly daily for 12 days.

[P1-S1] **Drops** containing the above quantities in 25 minims are prepared.

*Dose*.—8 to 10 drops in water after food twice a day (for adults). Maximum daily dose 25 drops.

[P1-S1] **Ferruginous Solution** (Duncan, Flockhart, Edinburgh). Ampoules for intramuscular injection containing iron cacodylate  $\frac{1}{10}$  gr., strychnine cacodylate  $\frac{1}{200}$  gr., sodium glycerophosphate  $\frac{1}{10}$  gr. in 1 ml.

[P1-S1] **Iron-Arsenic-Strychnine Compound G.L.** (Glaxo Laboratories, London) is a preparation in ampoules for injection as a tonic and in anæmia.

[P1-S1] **Sodii Cacodylas** (B.P.C., *P. Helv. V, Fr. Cx., P.G. VI, U.S.P. XI, P. Ital. V, F.E. VIII, P. Belg. IV*).

*Syn.* SODIUM DIMETHYLARSONATE.  $(CH_3)_2AsO_2Na, 3H_2O = 214.0$ .

*Dose*.— $\frac{1}{4}$  to 1 grain (0.016 to 0.06 g.) orally, per rectum or hypodermically. When given orally an alliaceous odour is imparted to the breath; the odour is less marked when the compound is given by injection.

*Fr. Cx.* has max. single dose  $1\frac{1}{2}$  grains and max. during 24 hours 3 grains approximately. *P. Helv. V* has  $1\frac{1}{2}$  and 5 grains respectively for oral administration and 3 and 10 grains respectively for hypodermic injection.

A white, odourless, crystalline or granular powder, very deliquescent.

The salt of the above formula contains 35% of As whilst the anhydrous salt contains 46.8%, equivalent to 61.8% arsenious acid.

*Soluble* 2 in 1 of water, 1 in 1 of alcohol 90%.

**Uses.** In tuberculosis generally (curative results very slow), exophthalmic goitre, pernicious anæmia, malaria, chorea, psoriasis and other chronic skin affections, and in all cases in which arsenic has been used, but when given by the mouth or per rectum may cause renal congestion with albuminuria and fall in the quantity of urine excreted. The usual dose in syphilis is 1 to 2 gr. intramuscularly *per diem* for a week or 10 days. Some prefer 3 gr. daily for 7 days, then 1 gr. doses subcutaneously.

**DISSEMINATED SCLEROSIS.** Good results with  $\frac{1}{2}$  gr. doses injected daily or every other day for 12 to 14 days. Courses of injections at 3-monthly intervals.

**ENDOCARDITIS** treated by daily intravenous injections beginning with 1 gr. and increasing gradually to 5 gr. Free from ill effects.

**FURUNCULOSIS.** Sodium cacodylate hypodermically on alternate days rapidly clears up furunculosis.

**MALARIA** well treated by intravenous injections of 30 gr., divided into 4 doses of  $7\frac{1}{2}$  gr. at 6-hour intervals, until parasites have disappeared from peripheral blood, when dose is halved and continued for a fortnight.

**PEMPHIGUS** of acute type responds to 2 gr. doses. Total 50 gr. during 5 weeks.

**PERNICIOUS ANÆMIA.** Sodium cacodylate  $\frac{1}{2}$  gr. may be given hypodermically daily for 20 days.

[P1-S1] **Injectio Sodii Cacodylatis.** A sterile preparation containing the equivalent of 0.05 g. ( $\frac{1}{20}$  grain) of cacodylic acid in 1 ml. (15 minims approx.). The same dose diluted with 4 drachms of water is used for rectal injection.

[P1-S1] **Injectio Cacodylatum Compositum.** *Dose* (average).—15 minims (1 ml.), containing sodium cacodylate  $\frac{1}{2}$  gr., iron cacodylate  $\frac{1}{2}$  gr., strychnine cacodylate  $\frac{1}{8}$  gr. It should be rendered slightly acid with cacodylic acid. 1 ml. contains approx. 0.03 g. ( $\frac{1}{2}$  gr.) of As.

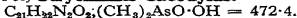
[P1-S1] **Cyto-Sol** (*Corbière, Paris; Anglo-French Drug Co., London*). Ampoules of 5 ml. contain sodium cacodylate 0.3 g., strychnine sulphate 0.001 g. in isotonic saline. *Dose*.—5 ml. intramuscularly or intravenously daily or every other day.

[P1-S1] **Hemo-Cyto-Sol** (*Corbière, Paris; Anglo-French Drug Co., London*). Colloidal iron 0.01 g., sodium cacodylate 0.3 g., strychnine sulphate 0.001 g., isotonic saline 5 ml. *Dose*.—5 ml. intramuscularly daily or every other day.

[P1-S1] **Optarson** (*Bayer Products, London*). Solution of ammonium heptin-chlorarsonate and strychnine nitrate. *Dose*.—1 ml. subcutaneously (= 0.004 g. of  $\text{As}_2\text{O}_3$  and 0.001 g. of strychnine nitrate). Tonic.

[P1-S1] **Strychnokodyl** (*Richter, London*). Issued in two strengths; A contains sodium cacodylate  $\frac{1}{2}$  gr., strychnine  $\frac{1}{125}$  gr., in 1 ml., B contains  $\frac{1}{2}$  gr. and  $\frac{1}{125}$  gr. respectively. *Dose*.—1 ml. subcutaneously on alternate days. General tonic and stimulant and in alcoholism.

### [P1-S1] Strychnine Cacodylas.



*Dose*.— $\frac{3}{32}$  to  $\frac{1}{16}$  grain (0.002 to 0.006 g.), usually by injection.

White crystalline powder hardly **soluble** in water, readily soluble in chloroform. Has proved a useful salt.

[P1-S1] **Sérum Névrosthénique Ampoules** (*Fraisse, Paris; Wilcox, Jozeau, London*) contain 0.1 g. of sodium glycerophosphate and 0.0005 g. of strychnine cacodylate, for hypodermic injection. In neurasthenia and other nervous affections. *Dose*.—1 ampoule daily for 12 days.

[P1-S1] **Drops** are also prepared for use by the mouth, containing the above quantities in 25 minims. *Dose*.—25 drops daily.

### [P1-S1] Di-sodii Methylarsonas (*F.E. VIII, P. Ital. V*).

*Syn. and Prop. Name.* SODIUM METHYL ARSONATE (*Fr. Cx.*), SODIUM METHARSINITE, ARRHENAL (*Adrian, Paris*), "NEW CACODYLE."  $\text{AsO}(\text{CH}_3)(\text{ONa})_2 \cdot 6\text{H}_2\text{O} = 292.0$ . *P. Belg. IV* has  $5\text{H}_2\text{O}$ .

*Dose*.— $\frac{1}{2}$  to 2 grains (0.03 to 0.12 g.) *per os* or hypodermically. *Fr. Cx.* has max. single dose  $1\frac{1}{2}$  grains; max. in 24 hours, 3 grains.

Prepared by the interaction of methyl iodide and sodium arsenate in presence of excess of alkali. In white crystalline powder containing (with  $6\text{H}_2\text{O}$ ) 25.65% of As.

**Soluble** about 1 in 1 of water, only slightly in alcohol 90%.

**Uses.** Similar to sodium cacodylate, *q.v.*

It is stated not to produce cacodyl oxide when given by the mouth.

[P1-S1] **Enesol** (*Clin Laboratories, Paris; Mertens, London*), is MERCURY SALICYLARSONATE, a combination of disodium methylarsonate and mercury salicylate. A white powder containing 36% mercury. It is best supplied in solution. This is said to be painless on injection.

*Dose*.— $\frac{1}{2}$  to 1 grain (0.015 to 0.06 g.) intramuscularly.

Syphilis and parasyphilis are treated by 2 ml. of 3% solution (= 1 grain approx.) intramuscularly once daily, or for intensive treatment of syphilis 4 to 8 ml. every 2 or 3 days. Intravenously, 4 to 10 ml. every 2 or 3 days according to urgency. When a total amount of 1.5 g. is reached, treatment should be suspended for 10 days.

General paralysis, malaria, and psoriasis, are also treated with it.

[P1-S1] **Arsylen** (*Roche Products, Welwyn Garden City*). Allylarsonic acid. In granules containing 0.01 g. in the form of calcium allylarsonate, or ampoules containing 0.05 g. as sodium allylarsonate. In skin and blood diseases, convalescence, etc.

## (II) Aromatic Series

[P1-81] **p-Aminophenylarsonic Acid.** *Syn.* ARSANILIC ACID, ANILINE-ARSENIC ACID.  $\text{NH}_2\text{C}_6\text{H}_4\cdot\text{AsO}(\text{OH})_2 = 217.0$ .

Arsanilic acid is weakly basic. Its hydrochloride is immediately hydrolysed by water. It is soluble in methyl and ethyl alcohols. It has been employed as:—

[P1-81] **Sodii Aminarsonas (B.P.C.).** *Syn. and Prop. Names.* SODIUM p-AMINOPHENYLARSONATE, SODIUM ARSANILATE, ATOXYL (*Boehden, Berlin*), SOAMIN (*Burroughs Wellcome, London*).  $\text{NH}_2\text{C}_6\text{H}_4\text{AsO}(\text{OH})\text{O}\cdot\text{Na} = 239.0$ . Contains a variable proportion of water, usually 3 to 4 molecules. *P. Belg. IV* requires  $3\text{H}_2\text{O}$ , *Fr. Cx.*  $4\text{H}_2\text{O}$ . *B.P.C.* requires 24 to 25.6% of As.

*Dose.*— $\frac{1}{2}$  to 3 grains (0.05 to 0.2 g.). This dosage *per os* for syphilis and chronic skin diseases has been advised daily for a week, then to be intermitted, but caution is recommended (*vide infra*). Max. single dose 3 grains (0.2 g.). It has also been given subcutaneously, intramuscularly and intravenously.

Many patients object to subcutaneous injections of Atoxyl on account of the pain. This may be avoided by dissolving the dose of Atoxyl in 10% solution of sodium citrate.—*M. Berté, per Trop. Dis. Bull., 1939, 671.*

Solutions should be freshly prepared with cold boiled water and may be slightly warmed at time of injection.

A white crystalline powder with slightly saline taste.

**Soluble** about 1 in 6 of water. Also soluble about 1 in 125 of alcohol 90% and more so in methyl alcohol. The anhydrous substance is readily soluble in methyl alcohol but practically insoluble in ether, acetone, benzene or chloroform.

**Incompatible** with mercurials (*e.g.*, perchloride), and other heavy metals in solution, also with acids.

**Uses.** This compound was first employed in the treatment of trypanosomiasis. Owing to the success achieved by its use in this condition it was subsequently employed in syphilis, malaria, relapsing fever, pernicious anæmia, elephantiasis and other diseases. Unfortunately, although the single dose is far less toxic than the equivalent amount of arsenic, its continued use over prolonged periods causes degenerative changes in the central nervous system leading to blindness and even to death, and its use has now largely been abandoned in favour of other preparations such as tryparsamide and neoarsphenamine, though it is still employed to some extent for its original indication, *i.e.*, trypanosomiasis.

[P1-81] **Sodii Acetylarsanilas (P.G. VI, P. Belg. IV).**

*Syn.* SODIUM ACETYLAMINOPHENYL-ARSONATE.

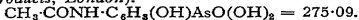
$\text{C}_6\text{H}_4\cdot\text{NHCOCH}_3\cdot\text{AsO}_3\text{HNa}, 4\text{H}_2\text{O} = 353.1$ . *P. Helv. V* has  $5\text{H}_2\text{O}$ .

*Dose.*—*Per os*  $\frac{1}{2}$  grain (0.03 g.) 3 or 4 times a day.

Colourless crystals. **Soluble** 1 in 10 of water, insoluble in alcohol.

This has been used similarly to sodium aminarsonate in trypanosomiasis, syphilis, etc., but is stated to be less effective therapeutically and to produce similar toxic effects.

[P1·81] **Acetarsol** (*B.P. Add. I*). *Syn. and Prop. Names.* ACET-ARSONE, 3-ACETYLAMINO-4-HYDROXYPHENYLARSONIC ACID (*Fr. Cx.*), FOURNEAU 270, STOVARSOL (*Pharmaceutical Specialities (May & Baker) Ltd., London*), KHAROPHEN (*Burroughs Wellcome, London*), ORARSAN (*Boots, Nottingham*), ORSANINE (*Société Parisienne d'Expansion Chimique, Paris*), SPIROCID (*Bayer Products, London*).



*Dose.*—1 to 4 grains (0.06 to 0.25 g.) for adults;  $\frac{1}{2}$  grain (0.03 g.) maximum for children. Stated to be readily absorbed from the gastro-intestinal tract.

Colourless crystals having a high As content (27% approx.) and low toxicity. It was introduced by Fourneau and Levaditi in 1922.

**Insoluble** in cold water, alcohol 90% and dilute acids; moderately soluble in boiling water and in alkalis, the corresponding salt being formed.

**Toxic symptoms** sometimes occur, e.g., diarrhoea, vomiting, headache and cutaneous eruptions. Exfoliative dermatitis has been reported following continued use.

Dermatitis, from administration of 40 gr. in 13 days, quickly subsided on giving 10 ml. intravenous injections of a 10% strontium bromide solution.—H. C. Semon, *Lancet*, ii/1932, 341.

Toxic erythema in 13, and peripheral neuritis in 2, out of 232 cases of amœbiasis treated. Risk of treatment considerable and particularly dangerous unless patient is under constant supervision.—P. W. Brown, *J. Amer. med. Ass.*, i/1935, 1321.

**Uses.** In amœbiasis, yaws, lambliasis, malaria, and the early treatment of syphilis. Has the advantage of being active when given orally. It is also employed both orally and intravenously in the treatment of neurosyphilis, though it may give rise to toxic reactions. It is effective in congenital syphilis, but should be used with caution.

Used with success in spirillary diseases, e.g., intestinal spirochætosis, ulcer-membranous-stomatitis, spirillary bronchitis, phagedenic ulcer, and Vincent's angina; also lesions resistant to arsphenamines.

In acute cases of amœbiasis destruction of cysts entails dosage of 8 gr. per day for 10 days. Stated to cure when emetine has failed. In chronic cases, 4 gr. the first day, later 4 gr. every other day for a week, then twice a week for several weeks. (For the combined treatment with Auremetine, v. p. 663.)

The combined treatment of amœbic dysentery (in France) with acetarsol and emetine lasts 4 weeks and consists of administration of 0.5 g. of acetarsol a day during 1st and 3rd weeks, and emetine during 2nd and 4th weeks. The "opening" treatment with acetarsol alone consists of administration of 0.75 g. a day for one week, discontinued following week and resumed on 3rd week, followed for one or two months by daily dose of 0.25 g. Amœbæ disappear in 4 days and cysts in 8 days.

In yaws the following has been advised: Two 4 gr. tablets the first day, three the second day, four the third day. Omit for one day, then four, three and two tablets respectively on alternate days.

For lambliasis, one 4 gr. tablet a day for six days. The dose may be doubled and treatment extended, in cases with cysts. The dosage for children should be *pro rata*. Improvement with disappearance of cysts. Blastocysts, the cause of diarrhoea, destroyed.

In malaria 15 gr. *per os*, in a single dose, will free the blood of tertian parasites but does not affect malignant or quartan forms. It is said to be a useful adjuvant to quinine.

**CONGENITAL SYPHILIS.** While acetarsone is effective in the treatment of congenital syphilis the effective dose is so near to the dose that causes severe reactions that its indiscriminate employment is felt to be unwise. Maxwell and Glaser report a death after 7.68 g. of acetarsone over a period of 84 days.—H. N. Cole, *J. Amer. med. Ass.*, i/1937, 825.

**DIPHTHERIA.** Successful results in disinfection of 47 infant carriers of diphtheria by nasal instillation thrice daily for five days of a 10% watery suspension of Spirocid. From one to three such series of treatments are commonly required. Only one child showed toxic symptoms, consisting in morbilliform and erythematous eruptions.—A. Iancon *et al.*, *per Brit. med. J. Epit.*, i/1937, 2.

**NEUROSYPHILIS.** Good results reported from *intravenous* injection of Stovarsol. Solution prepared by dissolving 1 g. in 9 ml. of 4% sodium hydroxide and adding 11 ml. of distilled water. Initial dose 0.5 g. and succeeding doses 1 g. at weekly intervals.—L. H. Griggs and J. F. Schamberg, *Arch. Derm. Syph.*, N. Y., 1934, 645.

Oral administration of Stovarsol in cases of neurosyphilis certified as insane. The serological results in 22 cases warrant further trial. Clinical results, though favourable in some cases, do not at present justify any conclusions. The drug was given on alternate weeks, the number of tablets given daily being regulated approximately by the body weight, patients of 11, 9 and 7 st. receiving respectively 5, 4 or 3 tablets (each 4 gr.). Toxic effects may be produced, requiring the use of calcium thiosulphate as an antidote, but the insidious onset of blindness, sometimes observed with Tryparsamide, is a rare complication.—R. Fakenham-Walsh, *Lancet*, i/1937, 982.

**VINCENT'S ANGINA.** The most rapid cure is obtained by the use of a thick paste, prepared by triturating a tablet of 0.25 g. in a few ml. of water or glycerin which is massaged into the gums. Tablets of the same dose are also given three or four times (half doses for children).—C. H. Maxwell, *per Practitioner*, ii/1936, 660.

**YAWS.** Yaws is as difficult to cure as syphilis. It is true that the lesions of yaws are easily healed with a few doses of arspenamine and that bismuth compounds are also effective, but to say that this means that the disease is easily cured is as fallacious as the statement would be if applied to syphilis. If one is to be guided by the number and frequency of relapses and by the persistently positive serologic reactions one feels inclined to say that yaws is incurable in a large proportion of cases and that the treatment should be, as for syphilis, vigorous and continuous. In Cuba the treatment for patients with yaws is the same as that for syphilis, but where continuous treatment by injection is not practicable, successful therapy was instituted with acetarsone tablets in a dose of 0.25 g. daily for 20 days, these courses of treatment being repeated at least three times with intervals of two weeks of rest.—V. Pardo-Castello, *Arch. Derm. Syph.*, N. Y., 1939, 40, 772.

**[P1-S1] Acetarsol Sodium.** *Syn. and Prop. Names.* SODIUM ACETYLAMINOHYDROXYPHENYLARSONATE (*Fr. Cx.*), ORSANINE-SODIUM (*Société Parisienne d'Expansion Chimique, Paris*), STOVARSOL-SODIUM (*Pharmaceutical Specialities (May & Baker) Ltd., London*). A white powder soluble 1 in 8 of water.

For injection in yaws, general paralysis and malaria.

Ampoules contain 0.5, 1 and 1.5 g., injections being given three times a week until a total of 20 g. has been given.

[P1-81] **Devegan Vaginal Tablets** (*Bayer Products, London*). Acetarsol and boric acid with carbohydrate hydrolysed by a special process. In leucorrhœa, especially that due to *trichomonas vaginalis*.

Review of results of 185 cases of vaginal discharge. Best results only obtained with in-patients. One to four tablets of Devegan inserted high in the vaginal fornices, at first twice daily and then at lengthening intervals, and finally just after the menstrual periods only. Desired result obtained in from 2 weeks to 2 months in two-thirds of the cases. Complete disappearance of discharge, or a substantial improvement, occurred in all but a small proportion of cases. Results definitely superior to antiseptic douches.—P. Hauptstein, per *Lancet*, i/1936, 382.

All but 7 of 47 patients clear of trichomonas infection after 3 months (and 5 of the 7 had an associated gonorrhœa). The tablets are more effectively inserted by an experienced person.—J. L. Collis, *J. Obstet. Gynec.*, Feb., 1936, 87.

The best results in trichomonas vaginitis have been obtained by the use of Devegan tablets; 2 tablets, inserted once or preferably twice daily and used in conjunction with an alkaline or a 1 in 1000 potassium permanganate douche, have relieved the condition quickly. It must be realised, however, that unless treatment is continued for from two to three months relapses are almost certain to occur.—E. W. Assinder, *Brit. med. J.*, i/1936, 882.

In hypersensitive patients arsenical intolerance may arise from the local use of arsenical preparations in the treatment of *trichomonas vaginalis* infection. A case described.—C. G. H. Campbell, *Lancet*, ii/1937, 688.

A case of severe dermatitis following use of vaginal tablets for *trichomonas vaginalis* infection. This result was not due to hypersensitivity, but to adsorption over a period of seven weeks, owing to the fact that the daily vaginal douche was omitted. The skin condition cleared up on cessation of the treatment.—M. C. W. Long, *Lancet*, ii/1937, 828.

[P1-81] **Stovarsol Vaginal Tablets** (*Pharmaceutical Specialities (May & Baker) Ltd., London*) are used for similar purposes.

[P1-81] **Bistovol** (*Pharmaceutical Specialities (May & Baker) Ltd., London*). The bismuth salt of acetarsol, in ampoules containing 3 ml. of 10% suspension in oil. For adults a series of 12 injections of 1.5 to 3 ml. at intervals of 4 to 5 days is suggested.

Primary and secondary syphilis well treated by Bistovol *per os* either in solution or tablets. Well tolerated in doses of 2 g. daily for 8 to 11 days. Rapid disappearance of spirochaetes and prompt cicatrization of lesions.—C. Levaditi and L. Fournier, *Lancet*, i/1928, 697.

[P1-81] **Acetylarsan** (*Pharmaceutical Specialities (May & Baker) Ltd., London*).

Diethylamine acetarsol, a white crystalline powder, soluble in water. Two solutions are prepared: (1) for adults, containing 23.6% of active product, 1 ml. of which is equivalent to 0.05 g. of arsenic; and (2) for children weighing less than 15 kg., containing 9.4% of active product, 1 ml. of which equals 0.02 g. of arsenic (the basis of dosage with this solution is 0.15 ml. per kilo body weight). It is given subcutaneously or intramuscularly, the dosage in adults (after two preliminary injections, one of 1 ml. and one of 2 ml.) being 3 ml. given at three-day intervals, a course consisting of 16 injections with an interval of one month between courses. Alternatively 5 ml. may be given, once a week for 8 weeks (not more than 3 ml. at one site). Indicated in all stages of syphilitic infection, in neurosyphilis, congenital syphilis, and in yaws. Used in hepatitis with success—dose, 0.75 g. once a week for 4 weeks. Also used, in conjunction with emetine, for amebiasis.

Effect on *S. pallida* equal to that of the arsenobenzenes, and serological effect compares favourably. More frequently followed by minor toxic effects than the arsenobenzenes.—V. E. Lloyd, *Lancet*, i/1928, 1323.

[P1-81] **Parosan** (*Pharmaceutical Specialities (May & Baker) Ltd., London*).

8-Acetyl-amino-3-hydroxy-1:4-benzisoxazine-6-arsonic acid. Has some analogy with Stovarsol and Tryparsamide. Tablets contain 4 gr. In disseminated sclerosis and neurosyphilis. Of little use in early syphilis.

[P1-81] **Carbarsonne**.  $\text{NH}_2\text{CONH}\cdot\text{C}_6\text{H}_4\text{AsO}(\text{OH})_2 = 260.07$ .

*Syn. and Prop. Names.* *p*-CARBAMINOPHENYLARSONIC ACID, AMEBEVAN (*Evans, Sons, Lescher & Webb, Liverpool*), LEUCARSONE (*Pharmaceutical Specialities (May & Baker) Ltd., London*).

*Dose.*—0.25 gramme twice daily for 10 days.

A white crystalline solid without odour or taste, containing 28.85% of arsenic. M.p. 174°.

Practically *insoluble* in water but dissolves in aqueous alkaline solutions.

*Uses.* Carbarsone is employed in the treatment of chronic intestinal amœbiasis. While it is said to be less toxic than acetarsol (and more amœbicidal), cutaneous and other reactions common to arsenic compounds have been observed and the possibility of optic injury, though not serious, should nevertheless be kept in mind. The arsenic is only slowly liberated and suitable intervals between courses should be allowed in order to avoid a cumulative effect; in common with other arsenicals it should not ordinarily be employed in the presence of hepatitis or kidney damage.

Carbarsone is usually administered by the mouth in a dose of 0.25 g. twice daily for a period of ten days, the course being repeated if necessary after an interval of a week or ten days. In resistant cases, or in cases with acute symptoms, it may be given as a retention enema, 2 g. of the drug being dissolved in 200 ml. of warm 2% sodium bicarbonate solution; this is given on alternate nights for a maximum of five doses. The retention enema is preceded by a cleansing alkaline enema. It is not advisable to give the drug by mouth concurrently with the rectal administrations.

It is non-toxic in clinically effective doses.—A. C. Reed and co-workers, *J. Amer. med. Ass.*, i/1932, 189-198. Apparently effective.—*ibid.*, 231.

Study of forty-four drugs in order to find one with low toxicity and high amœbicidal powers showed carbarsone to be the best. 0.25 g. given twice daily for ten days. In obstinate cases retention enema of 2 g. of carbarsone in 200 ml. of warm water with 1% of sodium bicarbonate; after preliminary cleansing, enema repeated on alternate nights for five treatments. No toxic symptoms—only slight epigastric discomfort reported.—H. H. Anderson, *J. trop. Med. (Hyg.)*, i/1933, 69.

Doses of 0.25 g. of carbarsone twice daily for 10 days with no untoward effects in 31 cases and with 23 cures reported by R. N. Chopra, B. and S. Sen, *Indian med. Gaz.*, 1933, 315.

200 ml. enemas of 1% carbarsone in 2% sodium bicarbonate last thing at night after a sedative of sodium amylal, repeated until they have been retained on five occasions, of value when the oral use of the drug had failed. In extensive trials orally and rectally in total quantities of 75 to 2100 mg. per kilo, over periods of up to 15 months, intolerance only noted in one case of hepatitis after 5 g. in ten days.—H. H. Anderson and J. C. Reed, *Amer. J. trop. Med.*, 1934, 257.

A total oral dosage of 3.0 g. per kilo over a period of 48 weeks has been employed with no perceptible harm.—H. A. Anderson, *J. trop. Med. (Hyg.)*, 1935, 272.

The therapeutic failures of the carbarsone treatment of amœbiasis were reduced from 10 to 3% by combining it with retention enemas of chiniofon. A single course of carbarsone was given in 104 cases, 0.25 g. before breakfast and supper for 10 days and enemas of 250 ml. of a 2.5% chiniofon.—J. G. Mateer [P1-81], *Amer. J. digest. Dis.*, 1940, 154.

[P1-81] **Amibiaron** (*Bengal Chemical & Pharmaceutical Works, Calcutta*). 4-carbamino-phenyl-arsenic acid. *Dose.*—0.25 grammes (in gelatin capsules) twice a day *per os* for 10 to 15 consecutive days. For the treatment of chronic intestinal amœbiasis.

Patients are kept on ordinary diet and a saline purgative is taken with the Amibiaron. Cure is recorded when 6 or more consecutive stools have been examined on different days and found negative in respect of *E. histolytica*. Of 40 patients who received this treatment 25 (62.5%) were cured; in 10 (25%) the result was indeterminate and in 5 (12.5%) it failed.—T. N. Chopra, B. Sen and G. Sen, *Indian med. Gaz.*, 1935, 324.



[P-81] **Tryparsamidum** (B.P. Add. I, U.S.P. XI, Fr. Cx.).  
*Syn.* SODIUM N-PHENYLGLYCINEAMIDE-*p*-ARSONATE (P. Ital. V),  
 GLYPHENARSINUM (P. Belg. IV), TRYPARSONUM (B.P.C.).

$\text{NaO}(\text{OH}) \cdot \text{AsO} \cdot \text{C}_6\text{H}_4 \cdot \text{NH} \cdot \text{CH}_2 \cdot \text{CONH}_2, \frac{1}{2} \text{H}_2\text{O} = 305.1$ .

(The U.S. patent, owned by the Rockefeller Institute, having expired on September 24th, 1935, the Institute dedicated the name tryparsamide to the public as a non-proprietary designation, and the Council on Pharmacy and Chemistry of the A.M.A. adopted the name as a non-proprietary name for the product.)

*Dose.*—15 to 30 grains (1 to 2 g.) by subcutaneous, intramuscular or intravenous injection. U.S.P. XI average dose 30 grains intravenously. Up to 45 grains may be given for a dose.

A white crystalline powder obtained by treating sodium *p*-aminophenylarsonate with chloracetamide and recrystallising the sodium salt of the acid thereby obtained. The anhydrous substance contains about 25% of As. It is required to comply with biological tests for freedom from toxicity.

**Soluble** 3 in 10 of water, forming a neutral solution; almost insoluble in alcohol, chloroform and ether.

**Uses.** Originally introduced for the treatment of trypanosomiasis, but is effective only against *T. gambiense* (African sleeping sickness); *T. rhodesiense* is not destroyed. Is now used also in neurosyphilis and is usually preferred to arsphenamine compounds in tabes and paresis. The best results seem to be obtained in patients with early dementia paralytica. It is liable to produce optic atrophy, and is contraindicated in neurosyphilis with optic neuritis. Has no effect on primary or secondary syphilis. It is a valuable follow-up treatment after malaria therapy in G.P.I. Should be given in courses of 8 or 10 weekly injections, the total dosage required being 20 to 40 g. in trypanosomiasis (more in chronic cases), and 130 g. or more in neurosyphilis. Injections are usually given intravenously. Toxic effects are indicated by ocular pain, lachrymation and photophobia.

**TRYPANOSOMIASIS.** In patients of the first stage, a total dosage of 20 to 40 g. usually cures, but in chronic cases 50 to 100 g. is necessary (Van den Branden). The best dosage for adults in good condition is 3 g. weekly, and in poor condition 2 to 3 g.; for children 0.5 to 2 g. Action is rapid, durable, constant, and superior to any other drug, relapses or incomplete cures being due to extraneous causes; toxic reactions are negligible, cases of total blindness recorded being due to previous arsenical treatment (Marugo).

The single course of 50 g. for an adult appears to cure 52% and to ameliorate greatly 48% in the second stage. Accidents insignificant and ocular troubles rare and not severe (Infante).—Abstracts of papers on the use of tryparsamide, per *Trop. Dis. Bull.*, Oct., 1928, 790.

Results of use in 1000 cases. Exerts unique action on advanced cases, but equally satisfactory in early cases.—Louise Pearce, *Rockefeller Inst. Monograph*, 1930; *Brit. med. J.*, ii/1930, 1094.

During 1934, 47,187 cases of sleeping sickness were treated in Nigeria, the great majority with a course of 20 to 25 g. of tryparsamide—initial dose 1 g., followed by 2 g. doses at 5-day intervals. Fewer toxic symptoms using distilled rather than boiled and filtered water. Antrypol (*see p. 1009*) became available towards the end of 1934, and patients are now being given 3 doses each of 1 g. of Antrypol, followed by a course of 9 to 11 g. of tryparsamide, with 5-day intervals between injections with both drugs.—H. M. O. Lester, *Report of the Tsetse Investigation*, per *Trop. Dis. Bull.*, 1936, 33, 169.

Lester found that toxic symptoms after tryparsamide only occurred when boiled and filtered water was used instead of distilled water. Routine treatment of trypanosomiasis in N. Nigeria now consists of three 1 g. doses of Bayer 205 or Antrypol, followed by five 2 g. doses of tryparsamide.—*Trop. Dis. Bull.*, 1940, 321.

**GENERAL PARALYSIS AND TABES.** In general paralysis, particularly megalomaniac forms, the prolonged use is worthy of trial. 1 to 2 g. doses given at weekly intervals intravenously.—M. Brown and A. R. Martin, *Lancet*, ii/1926, 699. See also *J. Amer. med. Ass.*, i/1927, 475.

The drug has no spirochætidal effect in man but has a local stimulating effect on the nervous system. In 37 cases of general paresis there was clinical cure or marked improvement in 63%, and serological cure or marked improvement in 75%. Clinical improvement depends very largely on the duration of the parenchymatous involvement and the degree of pre-existing damage. Tryparsamide appears capable of arresting the active syphilitic process but not of undoing the damage done. Optic injury is rarely produced after the tenth injection, and early and repeated examination of the eye is therefore essential.—F. E. Cormia, *Brit. J. ven. Dis.*, 1934, 99.

From observation of 155 patients with various types of syphilis of the central nervous system treated with tryparsamide and kept under rigid ocular control for a period of years, it is concluded that: (1) subjective reactions are not infrequent but are often due to suggestion; (2) severe objective signs of damage to the optic nerve occur infrequently with reasonable ocular control; (3) of patients treated with tryparsamide the percentage of those benefiting so far as the optic nerve is concerned is far greater than the percentage of those in whom damage may occur; (4) patients with optic atrophy due to syphilis should have the advantage of the use of tryparsamide when the drug is indicated.—L. L. Mayer, *J. Amer. med. Ass.*, ii/1937, 1793.

[P1-81] **Biarsamide** (*Pharmaceutical Specialities (May & Baker) Ltd., London*). Bismuth tryarsamide, containing 14.5% As and 40.5% Bi. Ampoules contain 2 or 5 ml. of 5% solution for intramuscular injection in nervous syphilis.

[P1-81] **Treparsol** (*Lecoq et Ferrand, Paris; Bengué, London*) (0.25 g. tablets). *Syn.* ACIDUM 4-OXY-3-FORMYLAMINOPHENYLARSINICUM (*P. Belg. IV*), FORMYPHENARSINE.

Treparsol is formyl-*m*-amino-*p*-oxyphenylarsonic acid, a white powder almost insoluble in water, alcohol and ether. For oral administration in syphilis.

[P1-81] **Neocryl**. *Syn.* SODIUM SUCCINANILOMETHYLAMIDE-*p*-ARSONATE. A white crystalline substance readily soluble in water. Rather less toxic than tryparsamide and has greater trypanocidal activity. Well tolerated in man, by intravenous injection of a 15 to 20% solution in sterile distilled water, in weekly amounts of from 2 to 4 g., the usual course consisting of the administration of this amount weekly up to a total of 30 to 36 g.; one patient had an uninterrupted course of 69 g. without showing toxic symptoms. Neocryl has a definite action on primary, secondary and tertiary syphilis, though in primary syphilis it is best combined with bismuth. In neurosyphilis and tabes it gave very satisfactory results; and of 11 cases of Nigerian trypanosomiasis treated by a single course, 10 became clinically normal and the other was improved.—Warrington Yorke and co-workers, *Brit. med. J.*, i/1936, 1042 (Report to Therapeutic Trials Committee).

For an account of the preparation and therapeutic activity of succinyl derivatives of *p*-arsanilic acid see G. T. Morgan and E. Walton, *J. chem. Soc., Lond.*, March, 1931.

**NEUROSYPHILIS.** A comparison in a series of 570 cases showed that Neocryl is in no way inferior to tryparsamide as a therapeutic agent, and that toxic effects from its use are much less common than with tryparsamide. Visual disturbance occurred in 47 out of 256 treated with tryparsamide, whereas only one case occurred in 314 treated with Neocryl.—A. O. F. Ross, *Brit. med. J.*, ii/1940, 283.

### (III) Bis-phenyl Nucleus Series

[P1-81] **Arsphenamina** (*B.P.C., U.S.P. XI, Fr. Cx.*). *Syn. and Prop. Name.* ARSENOBENZENE, ARSENOBENZOL (*P. Jap. V*), ARSENPHENOL-AMINE, AMINO-ARSENO-PHENOL, DIOXYDIAMINO-ARSENO-BENZENE DIHYDROCHLORIDE, SALVARSAN (*Bayer Products, London*) (*P.G. VI*), EHRLICH-HATA, or "606."

Arsphenamine consists mainly of the dihydrochloride of 3 : 3'-diamino-4 : 4'-dihydroxyarsenobenzene.

*Dose*.— $1\frac{1}{2}$  to 10 grains (0.1 to 0.6 g.), by intravenous injection. *U.S.P. XI average dose* 6 grains.

Therapeutic Substances Act, 1925.—Under this Act and the Statutory Rules and Orders issued under it in 1931, arsphenamine, commonly known as *Salvarsan*, and analogous substances used for the specific treatment of infective disease, are controlled by Licence, under the Minister of Health in England and Wales, the Scottish Board of Health in Scotland, and the Minister for Home Affairs in Northern Ireland, both with regard to manufacture and standards of strength, quality and purity.

The Standard Preparations of arsphenamine, etc., are kept in the National Institute for Medical Research, Hampstead. Biological tests and tests for stability are applied. The label must state that the contents have been tested in accordance with Regulations under the Act.

*Introduction*. Ehrlich and his assistants (notably S. Hata of Tokyo) conducted research which led finally to the introduction of arsphenamine for the treatment of syphilis and other affections. It was hoped the compound would effect a "sterilisation of the system."

Arsphenamine solutions kill protozoa *in vitro*, and the  $\frac{C}{T}$  ratio,

*Curative dose or sufficient to destroy all parasites*  
i.e., *Toxic dose or max. dose which patient can tolerate* for the substance is satisfactory. Ehrlich maintained that this ratio must be  $\frac{1}{2}$  or less for a drug to be of value in this type of disease.

*Note*.—The  
Chemotherapeutic Index (R) =  $\frac{\text{M.T.D.}}{\text{M.C.D.}} = \frac{\text{Max. tolerated dose.}}{\text{Min. curative dose.}}$

If it is fairly large (5 to 10), the minimum curative dose is sufficiently far removed in quantity from the maximum dose tolerated for the drug to be useful.

Arsphenamine is a bright yellow powder, freely mobile in contact with glass surfaces, and odourless except for a slight smell of ether. Theoretically it contains approximately 31.6% of As. The Therapeutic Substances Regulations require not less than 30% or more than 34%. It is available in ampoules, each containing 0.6, 0.5, 0.4, 0.3, 0.2 or 0.1 g. filled with inert gas to prevent oxidation. If discoloured—either grey or brownish—it must not be used.

*Soluble* 1 in 5 of water, forming a thick syrupy liquid with acid reaction, but not acid to congo-red paper, 1 in 3 of methyl alcohol, 1 in 12 of ethyl alcohol; also soluble in glycerin. Insoluble in ether.

### **Toxic Effects and their Treatment.**

Arsphenamine compounds in excess are all liable to damage capillary endothelium. In the dosage commonly employed a wide variety of toxic manifestations may occur. *Vasomotor symptoms* of an anaphylactic nature ("nitritoid" reactions) may occur during or immediately after the injection, and last for about 30 minutes, rarely longer. For treatment, 10 to 15 m. of adrenaline solution should be given subcutaneously. These toxic symptoms may be

avoided by careful preparation of the solution and by slow administration.

**Rigor and headache**, diarrhoea and cramp in the legs may occur. They are usually due to faulty diet. All patients should fast for at least two hours before injection.

Late effects, including stomatitis, erythema, exfoliative dermatitis, headache, lassitude and possibly jaundice and cerebral disturbances may come on at periods varying from a few days to a few weeks. Stomatitis is more common in patients treated with mercury or bismuth in addition to arsenic. Headache and lassitude are indications for a break in treatment. For the dermatitis, sodium thiosulphate is given intravenously or intramuscularly (0.45, 0.6, 0.75 and 0.9 g.) on alternate days with 25 ml. of 25% dextrose intravenously on each of the intervening days. 30 gr. doses orally may also be given. Liver extract is also often very beneficial. Jaundice is rarely severe but may cause death. A high fat and high protein diet with low carbohydrate is useful for prevention. For treatment, intravenous injections of 25 ml. to 50 ml. of 25% glucose should be given daily.

Some authorities recommend routine injection of sodium thiosulphate before treatment with arsphenamine compounds. More recently ascorbic acid (*q.v.*) has been used with success in the treatment of dermatitis due to arsphenamine.

Cerebral symptoms are rare but usually fatal. Prompt treatment by phlebotomy to 20 oz., removal of 15 ml. of cerebrospinal fluid, and injection of 1 ml. of solution of adrenaline may be successful, the lumbar puncture being repeated if symptoms continue.—L. W. Harrison, *Price's Practice of Medicine*, 4th Edn., 1934.

Atropine  $\frac{1}{2}$  gr. hypodermically is also advised for immediate vasomotor reactions. The cardiac reactions are best treated with hypodermic injections of strychnine  $\frac{1}{64}$  gr., ether 30 m., or camphor  $1\frac{1}{2}$  gr.—P. Power, *J. R. Army med. Cps*, Jan., 1927, 46.

In the 17-year period 1919-35 there were 63 deaths in the United States Navy following the administration of the arsphenamines. Neoarsphenamine caused the largest number (34) of the deaths, which was to be expected, as this is the arsenical most extensively used in the Navy. None of the patients died after the first injection of an arsenical; 12 died after the second; 23 after 5 injections or less; and 20 had received more than 6 injections. Autopsies were performed on 44 cases, the results of which are presented and discussed. The striking findings were frequent hæmorrhages and œdema in the various organs of the body.—S. S. Cook, *Publ. Hlth Rep., Wash.*, 1936, 929.

**Contraindications.** Addison's disease, hæmophilia, severe visceral disease. Small initial doses and extra caution are necessary in alcoholism, cachexia, renal or cardiac lesions and where there is a tendency to eczema, also in diabetes since arsphenamine compounds increase the amount of blood sugar.

**Uses.** The acidity of arsphenamine must be neutralised at the time of use; it has been largely replaced by neoarsphenamine, which needs only to be dissolved in water when required for use. The compounds are similar in effect and the description of uses, etc., below applies also in a large measure to the latter. Combined treatment with mercury or bismuth in addition is now more usual than treatment with arsenic alone.

Arsphenamine is usually given intravenously by the gravity method. Intramuscular injections, into the gluteal muscles, are now little used on account of the pain produced. Sulpharsphenamine has superseded it for that route.

A syphilitic chancre, a secondary syphilide or ulceration, or a tertiary gumma or ulceration, yields remarkably to the arsenicals. They are also of value in acquired or congenital syphilis. While arsphenamine, and more particularly neoarsphenamine, may be found of value in the early stages of neurosyphilis, other arsenicals, such as silver arsphenamine or tryparsamide are now more frequently employed.

Arsphenamine compounds are also used in malaria, septicæmia, relapsing fever, rat-bite fever, and yaws, and as a local application in Vincent's angina.

*Preparation of the Injection.*—Dissolve the dose in about 10 ml. of sterile water and make it alkaline by adding normal caustic soda solution (40 g. per litre), using the amount on the label required to dissolve the dose. (*U.S.P. XI* directs the addition of 0.85 ml. of N sodium hydroxide solution for each 0.1 g. of arsphenamine.) A precipitate is formed which re-dissolves on shaking. Dilute with normal saline so that each 0.1 g. is contained in approx. 20 ml. of solution. Injection is usually through one of the veins of the fold of the elbow, *e.g.*, the median cephalic, but any prominent vein may be used.

*Dose.*—0.1 to 0.6 g. Early syphilis is generally treated with from 0.2 to 0.3 g., and a number of injections, at intervals of a few days, gradually increasing up to 0.6 g., are given, with a total of 4 to 5 g. This course is usually *repeated* after an interval varying from 4 to 6 weeks, and *three or four such courses* are generally required. No food should be taken for two hours before or after the injection and alcohol should be forbidden. A mild purgative before the injection lessens the liability to untoward reactions. *Children* may receive from 0.02 to 0.2 g., according to age, but sulpharsphenamine subcutaneously, or neoarsphenamine intravenously, are preferable in such cases.

*"Combined Treatment"* with mercury, *vide postea*.

Patients should be treated in bed and observed for at least three days. If patient shows any signs of collapse during administration, the injection should be stopped at once.

### League of Nations Recommendations.

An enquiry in five countries (Denmark, France, Germany, Gt. Britain and the U.S.A.), carried out under the auspices of the Health Organisation of the League of Nations, into the treatment of syphilis in selected clinics. Statistical material was obtained from 94 clinics with 25,623 cases. As a result of the enquiry the following recommendations were made.—*Quart. Bull. Hlth Org. L. o. N.*, 1935, *I*, 239.

1. Treatment as early as possible in the sero-negative primary stage.

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2. Prior to treatment, there should be an adequate physical examination to determine the absence or otherwise of any indication for caution in dosage.

3. In carrying out the treatment, a strict supervision of the patient should be exercised, especially in respect of mucous membranes, skin, kidneys and liver.

4. Observations, clinical and serological, after completion of treatment should be for not less than three years.

5. Adequate examination of the spinal fluid, at least before dismissal from observation, is essential.

6. The principles to be followed in carrying out the actual treatment should be as follows: (a) To employ a comparatively heavy individual dosage of the arsenobenzene and of the bismuth or mercurial compounds, the doses being administered in comparatively rapid succession, especially at the commencement; (b) to maintain a persistent attack on the disease, avoiding intervals of such length as to afford the parasite an opportunity of recovering; (c) to administer approximately as much treatment to primary as to secondary cases.

A system either of intermittent treatment or of continuous treatment can be expected to yield satisfactory results in ordinary cases of early syphilis. (*For full details of these treatments see Vol. I, 21st Edn.*)

[P1-81] **Stabilarsan** (*Boots, Nottingham*). A stable compound of arsphenamine and glucose for intramuscular or intravenous injection supplied ready for use, as an approximately 10% solution in 50% glucose. Ampoules contain 0.05, 0.1, 0.15, 0.20, 0.30, 0.45, 0.6, 0.75 and 0.9 g. Doses larger than 0.45 g. should not be given intramuscularly.

In congenital syphilis the preparation is stated to be safe. For an infant 15 lbs. weight dose 0.075 g. (0.75 ml. of the solution in the ampoule). For routine treatment of syphilis a course is given combined with potassium iodide on the lines of arsphenamine methods. Has also been used with success in Vincent's angina, disseminated sclerosis and lymphadenoma.

[P1-81] **Arsphenamina Argentica** (*B.P.C.*). *Syn. and Prop. Name.* SILVER ARSPHENAMINE, SILVER ARSENOBENZOL, SILBERSALVARSAN (*P.G. VI*), SILVER SALVARSAN (*Bayer Products, London*).

*Dose.*— $1\frac{1}{2}$  to 10 grains (0.1 to 0.6 g.) intravenously in 1% solution, one or two injections of 0.1 g. each, then 0.2 g. for women, and 0.25 g. for men at intervals of not less than 4 days. Repeated at intervals until clinical symptoms and blood test satisfactory. In weakly patients begin with 0.05 g.

The sodium salt of silver 3 : 3'-diamino-4 : 4'-dihydroxyarsenobenzene. It is a brownish-black powder, containing 18 to 21% of As and 12 to 13% of Ag, readily *soluble* in water, with alkaline reaction. Ampoules contain 0.05, 0.1, 0.15, 0.2, 0.25 and 0.3 g.

Clinically 0.1 g. corresponds to about 0.2 g. of arsphenamine or 0.3 g. of nearsphenamine. It is thought to have the combined effect of arsphenamine and silver against syphilitic parasites. Mercury to be suspended during treatment. It is used especially for syphilis of the central nervous system, and must be given

very slowly to avoid vasomotor disturbances. It has also been employed with success in the treatment of disseminated sclerosis, the course consisting of three injections of 0.05 g. and three of 0.1 g.

**Contraindications.**—As for arsphenamine.

**TRICHINOSIS.** Six to 10 intravenous injections of silver arsphenamine make up the treatment usually required. Commencing with 0.05 g. the dose is increased with 0.05 g. each time until the dose of 0.30 g. is reached, then descended, decreasing the dose in the same proportion. The patients regained lost weight, abdominal pains ceased and cheeks again showed healthy colour.—J. Ragany, *Med. Rec., N.Y.*, 1935, 142, 335.

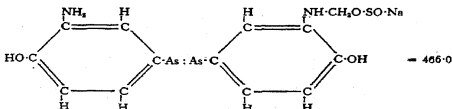
[P1-81] **Neoargentarsphenaminum** (*P. Helv. V*). *Syn. and Prop. Name.* NEOSILBERSALVARSAN (*P.G. VI*), NEOSILVER SALVARSAN (*Bayer Products, London*).

A molecular compound of neoarsphenamine and silver arsphenamine.

[P1-81] **Neoarsphenamina** (*B.P., U.S.P. XI, Fr. Cx., F.E. VIII, P. Belg. IV, P. Helv. V*). *Syn. and Prop. Names.* "914," NOVARSENO BENZENE, NOVARSENO BENZOL, N.A.B., NEO-ARSEN OBENZOLUM (*P. Jap. V*), NEOARSENPHENOLAMINE, NEO-KHARSIVAN (*Burroughs Wellcome, London*), NEOSALVARSAN (*P.G. VI*) (*Bayer Products, London*), NOVARSENO BILLON (*Pharmaceutical Specialities (May & Baker) Ltd., London*), NOVARSAN (*Synthetic Drug Co., Toronto; Allen & Hanburys, London*), NOVOSTAB (*Boots, Nottingham*), ARSEN OBENZOL ACID SODIUM FORMALDEHYDE-SULPHOXYLATE, SODIUM DIHYDROXYDIAMINOARSEN OBENZENE METHANESULPHONATE, NEOARSAMINOL (*P. Svec.*). The proper name under the Therapeutic Substances Act is Neoarsphenamine.

*Dose.*— $2\frac{1}{2}$  to 14 grains (0.15 to 0.9 g.) by intravenous injection. *U.S.P.* average dose 10 grains.

Consists mainly of sodium 3 : 3'-diamino-4 : 4'-dihydroxy-arsenobenzene-*N*-methylenesulphoxylate—



Neoarsphenamine is controlled by the Therapeutic Substances Act, 1925. It is made under licence and tested biologically (see Vol. II).

It is a yellow powder, readily *soluble* in water. The compound changes in the air, hence it is issued in sealed ampoules. The dry powder as taken from the sealed ampoules must contain not less than 18% or more than 21% of arsenic. The *B.P.* states that it contains approximately 20% of As. *Injections must be used immediately after preparation.*

**Manufacture.** Aqueous solutions of arsphenamine and formaldehyde sulphoxylate give a precipitate which is soluble in a

minute quantity of alkali to form an almost neutral solution. The product differs according to the temperature employed. At ordinary temperature the precipitate contains one "sulphur-acid" group.

**Uses.** Neoarsphenamine has almost entirely replaced arsphenamine owing to the ease with which solutions may be prepared—by simple solution in sterile water—and to the fact that it is less toxic. It is, however, also less toxic to spirochætes. Clinically it is found to have about two-thirds the activity of arsphenamine. It is given intravenously since intramuscular injections are painful, although the pain is reduced by using as solvent a solution of guaiacol 1, dextrose 50, sterile water to 100. For intramuscular injection sulpharsphenamine is more usual. Neoarsphenamine has been used in various diseases other than syphilis in place of arsphenamine. Its action in anthrax is stated to be almost specific, and good results are claimed for its use in the early stages of disseminated sclerosis. Vincent's angina and gangrenous balanitis are promptly arrested by a single intravenous injection of neoarsphenamine. Both arsphenamine and neoarsphenamine are specific in the treatment of yaws.

**Dosage.**—Many authorities recommend an initial intravenous injection of a small dose, *e.g.*, 0.45 g., followed by 8 to 10 doses at intervals of 3 to 8 days, gradually increasing the dose up to 0.75 or 0.9 g. as a maximum, repeating after an interval of 4 to 6 weeks. Three or four series may be required for complete treatment. Mercury or bismuth is frequently given during the intervals. 0.15 to 0.45 g. is given in from 5 to 10 ml. of water, or 0.6 to 0.9 g. in 15 to 20 ml. water, by slow injection into the median cephalic vein. More concentrated solutions have been employed, *e.g.*, 0.9 g. in 2 to 3 ml. water; concentrated solutions, however, require great caution.

*For contraindications and treatment of after-effects see Arsphenamina.*

**Intravenous drip therapy.** The massive dose method of chemotherapy employing intravenous drip therapy in early syphilis yields immediate clinical and serological results that equal the best results obtainable by the optimal methods of routine continuous treatment, and the course of therapy is measured in days rather than months. The intravenous drip is set up so that 5% dextrose is administered by the gravity method at the rate of about 100 ml. an hour. At the end of each hour there is added a solution of 0.1 g. of neoarsphenamine dissolved in 50 ml. of 5% dextrose.

In turn, this is followed by another hour of the plain dextrose, followed by another 0.1 g. of the drug until the total daily dose is administered. Thus, in a period of 15 hours a patient might receive 1500 ml. of 5% dextrose and 1 g. of neoarsphenamine. The treatment is started at 8 a.m. and continued throughout the day, the needle remaining *in situ*. In 86 male patients treated the average dose of neoarsphenamine was slightly in excess of 4.1 g. and the average duration of treatment slightly less than 5 days. Rapid healing of both primary and secondary lesions was noted and dark field examinations invariably became negative within 24 hours. In view of the toxic reactions, however, the treatment must still be considered in the experimental phase. A previous group of cases, similarly treated, and followed for a period of 5 years, appears to be clinically and serologically cured.—R. T. Hyman *et al.*, *J. Amer. med. Ass.*, ii/1939, 1208. (See also under Mapharside, p. 235.)



Preliminary Report of the Council on Pharmacy and Chemistry of the A.M.A. on the Chemotherapy of Syphilis by Massive Dose Intravenous Drip.—*J. Amer. med. Ass.*, ii/1940, 857.

**Combined Arspenamine and Mercurial (or Bismuth) Treatment.** (An analysis of records of 3598 cases treated at St. Thomas's Hospital V.D. Centre between January, 1920 and March, 1926.)

A course consisted of not less than 5 g. of an arspenamine compound (except with silver arspenamine, *q.v.*) with a minimum of 5 gr. of mercury or 2 g. of bismuth, intramuscularly or subcutaneously, over a period of not more than 4 months. With silver arspenamine a total of not more than 2.5 g. was given, with or without mercury or bismuth. A second course was given 3 months after the first and completed in 4 months.

The results of treatment with arspenamine compounds and mercury, compared with those with arspenamine compounds and bismuth, showed no superiority of bismuth over mercury, though bismuth was better tolerated. (The preparation of bismuth used was mainly the oxychloride suspended in glucose solution.) In sero-negative primary cases not less than two courses were necessary, and in sero-positive primary and early secondary cases even three courses did not give a satisfactory percentage of cures. Most relapses in early cases occurred in the first year, and a very small proportion after the second.

UNIT COURSE ON WHICH TREATMENT OF CASES ANALYSED IN REPORT WAS BASED.

Day.	Arsphen- amine comp. and Hg or grammes. grains. or Bi	grammes.	Day.	Arsphen- amine comp. and Hg or grammes. grains. or Bi	grammes.	
1	0.45	—	50	0.75	1	0.4
8	0.45	1	57	0.75	1	0.4
15	0.45	1	78	0.75	1	0.4
29	0.60	1	85	0.75	1	0.4
36	0.60	1	92	0.75	1	0.4

(Potassium iodide from 57th to 78th day.)

COURSE INSTITUTED 22/2/1928.

In this course the principle is to follow three short "bursts" of "914" (which ought effectually to destroy accessible spirochaetes) with three rests of a month each to allow liver cells and skin to recover, and to finish with two full courses of "914." The bismuth is crowded into the first 10 weeks to build up a depot.

Day.	Arsphen- amine comp. gram- mes.	Bi gram- mes.	Day.	Arsphen- amine comp. gram- mes.	Bi gram- mes.	Day.	Arsphen- amine comp. gram- mes.	Bi gram- mes.
1	0.45	0.4	43	0.75	0.4	85	0.90	—
8	0.45	0.4	50	0.90	0.4	92	—	—
15	0.60	0.4	57	—	0.4	99	—	—
22	—	0.4	64	—	0.4	106	—	—
29	—	0.4	71	—	—	113	0.90	—
36	—	0.4	78	0.90	—	120	0.90	—

—L. W. Harrison, *Spec. Rep. Ser. med. Res. Coun., Lond.*, No. 132, 1929.

**Whitechapel Course.** 1st to 5th week:—Intravenous neoarsphenamine 0.45 g. weekly; bismuth 0.2 g.; deep subcutaneous sulpharsphenamine 0.3 g. weekly; bismuth 0.2 g. 6th to 8th week:—Potassium iodide mixture 5 to 15 gr. thrice daily after meals. 9th to 13th week:—repeat as first 5 weeks. Patient to report for blood tests 7 days following last injection of course and again in 28 days and then given potassium iodide mixture until next course begins. A prophylactic draught of concentrated liver extract and glucose is given before each injection. Three courses are given at intervals of 8 weeks. In patients over 45, or with late syphilis, a course of intravenous injections once a week only, or deep subcutaneous injections once a week only, spaced as above, may be given. This course was primarily prepared for those in the acute infectious stages, but the patient's age is important.

The effects of treatment on 241 consecutive cases gave 236 Wassermann-negative within a month after first course of treatment. There were comparatively few complications (5·8%) and these were mostly mild cases of dermatitis.—T. Anwyl-Davies, *Brit. med. J.*, ii/1933, 487. Confirmed by 10 years' experience at the Seaman's Hospital, Liverpool.—A. O. Ross, *ibid.*, 585. Also by E. T. Burke, *ibid.*, 623.

*An analysis of the results of treatment of early, latent, and muco-cutaneous tertiary syphilis.* Based on the treatment at the Western Infirmary of Glasgow, of 1766 cases during the twelve-year period 1919-1932, a standard course of treatment having been adhered to throughout the whole period, and the technique of the Wassermann reaction remaining unchanged and under the control of one observer. The standard treatment employed throughout the investigation was the combined administration of "914" and a heavy metal. Results show that the prospects of radical cure are only good when treatment is commenced in the early stages of the disease, and even with existing methods of treatment many of the patients treated appear to be "cured" after two years treatment and observation. Chronic syphilis, however, cannot with certainty be cured, and thus any individual ought to undergo life-long observation.

The suggested first course should be:—

	"914" Bismuth metal			"914" Bismuth metal	
	g.	g.		g.	g.
1st day	0·45	0·2	19th day	0·60	0·2
4th day	0·60	0·2	26th day	0·60	0·2
8th day	0·45	0·2	33rd day	0·60	0·4
12th day	0·60	0·2	40th day	0·60	0·4
15th day	0·45	0·2	47th day	0·60	0·4

Thus 3·15 g. of "914" is given for primary penetration on the first 19 days and the amount of bismuth given amounts to 0·4 g. per week. A change from bismuth to mercury is suggested during the period between the courses of "914," and the mercury should be given intramuscularly. After the first course a period of four months will allow jaundice or evidence of skin intolerance to appear. After one month's rest eight weekly injections of calomel cream should be given. During this time potassium iodide may also be administered. Then a rest of 1½ months should be followed by a repetition of the first course. A third course is desirable in all cases of early syphilis and should be the same as the first two. The interval between the second and third courses should be extended to six months, and during this time ten injections of calomel cream will maintain the principles of continuous treatment. Thereafter the patient should be examined at two-monthly intervals and a Wassermann test of the blood should be performed. After two years, periodic examination should be made if possible at six-monthly intervals for as long as the patient will attend. A Wassermann test of the cerebrospinal fluid should be made at the end of the second year. In the event of an unfavourable Wassermann reaction at any time after the first course, at least one course should be given after the reversal of that unfavourable reaction.—W. R. Snodgrass and R. J. Peters, *Spec. Rep. Ser. med. Res. Coun., Lond.*, No. 224, 1937.

**SYPHILIS IN PREGNANCY.** Syphilis in pregnancy is treated on much the same lines as secondary syphilis, treatment being continued almost to the end of pregnancy, a careful watch being kept on the liver and kidneys. In the presence of albuminuria treatment by bismuth should be continued alone.

**CONGENITAL SYPHILIS IN CHILDREN.** Vary dose according to age of child: e.g., for child 1 month old, initial dose of N.A.B. 0·05 g., 1 to 3 years 0·1 g., and for older children 0·15 g., increasing during the course of six injections to respectively 0·1 g., 0·25 g., and 0·3 or 0·45 g., subsequent courses starting with larger doses and reaching higher maxima, but not exceeding 0·45 g. for a child of 12. For older children commence with 0·04 to 0·06 g. and increase up to 0·36 g. Injections are given intravenously or intramuscularly in from 1 to 3 ml. distilled water. (Alternatively, sulpharsphenamine intramuscularly may be employed, and is

frequently preferred.) Mercury is given either as Hyd. c. Cret.,  $\frac{1}{2}$  to 1 gr. thrice daily, or better still, the ointment rubbed in once a day, or as green iodide of mercury,  $\frac{1}{2}$  to  $\frac{1}{4}$  grain, 2 or 3 times daily during injections. In older children thirty or even forty arsenic injections may be necessary.

**Intraperitoneal injections** may be given with safety in infants suffering from congenital syphilis. A child of 10 lbs. should receive 50 mg., or 5 ml. of a solution consisting of 150 mg. of neoarsphenamine dissolved in 15 ml. warm sterile water. The usual treatment consists of 4 injections at 3-day intervals, followed by 4 injections at 7-day intervals, the ideal site for entrance of the needle being in the middle of the left rectus sheath, slightly below the level of the umbilicus. The method is not so rapid as intravenous injections, but neoarsphenamine is absorbed with sufficient rapidity to act in any condition. It is ideal for children with small veins needing urgent treatment.

#### References to use in other diseases.

**ANTHRAX.** N.A.B., 0.6 g. intravenously daily, or on alternate days, is specific; will save life and render surgical intervention unnecessary. Treatment generally adopted throughout S. Africa.—A. B. M. Thomson (Durban), *Brit. med. J.*, ii/1931, 921.

Report of a case so treated with success at St. Olave's Hosp., Rotherhithe.—J. J. Coghlan and H. J. Shorvon, *ibid.* Widely used in this country.—C. G. Brentnall, *ibid.*, 966.

Nine patients with pustular anthrax were treated with neoarsphenamine only. Seven of them made remarkable recoveries; the other two, aged 1 year and 5 years, died. The results suggest that neoarsphenamine, if given within four days of the appearance of the pustule, will almost certainly cure the disease.—F. W. Gilbert, *Lancet*, ii/1935, 1283.

**HERPES ZOSTER.** Neoarsphenamine hypodermically causes disappearance of pain in 3 to 4 hours and disappearance of eruption in a few days. Second injection rarely necessary.—Milian, *J. Amer. med. Ass.*, i/1929, 1024.

**LUNG AFFECTIONS, CHRONIC,** treated with intrapleural injection of Neosalvarsan. The pleura tolerates high dosage, 0.45 to 0.6 g. in 10 ml. water. It is a powerful antiseptic, especially against streptococci. It has been used in the bronchial tree in bronchiectasis.—*Lancet*, ii/1929, 32.

Intrathoracic injections valuable in suppurative lung conditions, e.g., gangrene, abscess, empyema and bronchiectasis. First aspirate pus and inject 0.15 g. Neosalvarsan, and repeat injection every 4 or 5 days, increasing to 0.6 g.—*Per Practitioner*, ii/1929, 155.

[P1-S1] **Pigmentum Neoarsphenaminæ** (*Mid. H.*). *Syn.* N. A. B. PAINT.

Neoarsphenamine 5, glycerin 50, water to 100. For Vincent's angina.

[P1-S1] **Neoarsphenamine Suppositories** (0.10 g. in cocoa butter) given to three months' old baby with hereditary syphilis, with good results.—E. G. Melon, *per J. trop. med. (Hyg.)*, Oct., 1922, 334.

[P1-S1] **Sulpharsphenamina** (*B.P., Fr. Cx., P. Ital. V, F.E. VIII, P. Belg. IV*). *Syn. and Prop. Names.* SULPHARSENOBENZENE, SULFARSENOL (*Sulfarsenol Laboratories, Alpertons; Modern Pharmacals, London*), KHARSULPHAN (*Burroughs Wellcome, London*), METARSENIBILLON (*Pharmaceutical Specialities (May & Baker) Ltd., London*), SULPHOSTAB (*Boots, Nottingham*), MYOSALVARSAN (*Bayer Products, London*), DI-SODIUM DIHYDROXY-DIAMINO-ARSENOBENZENE-DIMETHYLENE SULPHONATE. The proper name under the Therapeutic Substances Act is Sulpharsphenamine.

Described in the *B.P.* as consisting mainly of disodium 3 : 3'-diamino-4 : 4'-dihydroxyarsenobenzene-*N* : *N'*-dimethylene-bisulphite, but shown by Dyke and King to be a sodium salt of 3 : 3'-diamino-4 : 4'-dihydroxyarsenobenzene-*OO'N*-trimethylenesulphurous acid.

Sulpharsphenamine is controlled by the Therapeutic Substances Act, 1925, and Therapeutic Substances Regulations, 1931. It must comply with tests for toxicity, therapeutic potency and stability. It is a yellow powder soluble in water, giving a faintly acid solution in which gelatinous particles must not be visible. It contains approx. 20% of arsenic.

**Dose.**— $1\frac{1}{2}$  to 10 grains (0.1 to 0.6 g.) by subcutaneous or intramuscular injection, in fairly concentrated solution. The following is suggested as a course in primary syphilis for an average adult:—

	Water.		Water.
1st day 0.12 to 0.18 g. in 2 to 3 ml.		19th day 0.54 to 0.6 g. in 8 to 10 ml.	
3rd " 0.18 " 0.3 g. " 3 " 5 "		25th " 0.6 g. " 10 "	
5th " 0.30 " 0.42 g. " 5 " 7 "		40th " and later, Wassermann	
8th " 0.42 " 0.6 g. " 7 " 10 "		40th to 60th day, Arphenal.	
13th " 0.48 " 0.6 g. " 8 " 10 "		61st day, new series of injections.	

It is supplied commercially in a range of doses.

**Toxic Effects and Contraindications.** As for arsphenamine. It sometimes induces purpura hæmorrhagica and occasionally aplastic anæmia.

Death following intravenous administration of sulpharsphenamine.—J. R. Williams, *J. Amer. med. Ass.*, ii/1929, 1096.

**Uses.** It is less toxic than arsphenamine, and is used particularly for intramuscular injection because of freedom from pain. It is recommended for the treatment of congenital syphilis in infants, commencing with 0.05 g. for an infant 1 to 2 months old. Mercury should also be given either as grey powder orally,  $\frac{1}{2}$  to  $\frac{1}{2}$  gr., or by inunction with mercury ointment. Sometimes given intravenously, but this is not advisable. It is stated to have given good results in other diseases such as gonorrhœa, arthritis, rheumatism, hyperkeratosis and epididymitis.

[P1-S1] **Pigmentum Sulfarsenol** (*Sulfarsenol Laboratories, Alpertons; Modern Pharmaceuticals, London*). A 3% solution of Sulfarsenol in glycerin for use as a paint, mouth-wash or gargle in infections of the mouth and throat, such as Vincent's angina, stomatitis, gingivitis, etc.

[P1-S1] **Bismarsen** (*Abbott Laboratories, London*). Described as bismuth arsphenamine sulphonate or sulpharsphenamine bismuth. It is a precipitation compound made by adding bismuth potassium tartrate to sulpharsphenamine and pouring the solution, made by means of soda, into methyl alcohol. A yellowish soluble compound with arsenic content 13% approx. and bismuth content 24%.

**Dose administered intramuscularly.** *Initial dose.*—0.1 g., followed by doses of 0.2 g. in 1 ml. of sterile water, to which is added 2 minims of Butyn 2% as a local anæsthetic. Weekly doses at first, then 2 injections weekly for 20 injections. Repeat the course after an interval of a week. Children over 5 tolerate adult dosage well. Of value in early syphilis. Toxicity low and reactions benign and controllable.

It is said to be somewhat slower in action than sulpharsphenamine intramuscularly or nearsarsphenamine intravenously, and there may be some pain at the site of injection.

Criticism of the compound.—E. Tytler Burke, *Lancet*, i/1931, 1127.

Early syphilis treated with Bismarsen 0.1 to 0.2 g. intramuscularly.—Stokes, Miller and Beerman, per *Brit. med. J. Ept.*, i/1931, 110.

[P1-S1] **Mapharside** (*Parke, Davis, London*). *Syn.* MAPHARSEN.  $\text{HCl} \cdot (\text{NH}_2) \cdot \text{C}_6\text{H}_4(\text{OH})\text{AsO}_2 \cdot \frac{1}{2}\text{C}_2\text{H}_5\text{OH} = 258.53$ .

**Dose.**—0.04 g. intravenously as an initial dose for men, increased to a maximum of 0.06 g. Injections should be given every four or

five days, since it is rapidly excreted by the kidneys. For women the initial dose is 0.03 g., increasing to 0.04 g. for subsequent doses.

Mapharside is the semi-alcoholate of *m*-amino-*p*-hydroxyphenylarsine oxide hydrochloride. It is a white amorphous, odourless powder containing approximately 29% of trivalent arsenic.

**Soluble** in water, alcohol, acids and alkalis.

**Uses.** Mapharside is indicated in all forms of syphilis amenable to treatment by the arsphenamines, but is much less toxic and gives rise to less severe reactions. It is especially valuable in early syphilis.

Over a period of 18 months 233 persons were given 4666 intravenous injections of Mapharsen, the usual dose being 40 to 60 mg. (without addition of bismuth or mercury). Healing of visible lesions was rapid, comparing favourably with arsphenamine. Wassermann reaction reversed to negative in nearly all cases of early syphilis, but in half of the cases there was serological relapse. Clinical relapse and return to positive serological findings occurred most frequently after irregular or short periods of therapy. Nitritoid reactions were not observed, but mild gastro-intestinal disturbances were not uncommon and Herxheimer reactions were occasionally noted. Mild jaundice occurred in four cases and increase of renal impairment in four others.—Foerster and co-workers, *Arch. Derm. Syph.*, N.Y., Dec., 1935, 868.

Severe reactions such as exfoliative dermatitis and jaundice seem to be rare.—*Brit. med. J.*, ii/1936, 1038.

As the result of the administration of 15,000 intravenous injections of Mapharsen to 1400 patients with syphilis it was concluded that Mapharsen is as efficient as the arsphenamines. Reactions were minimal, mostly gastro-intestinal; no case of nitritoid reaction, hepatitis or exfoliative dermatitis was seen.—L. E. Schmidt and G. G. Taylor, *Amer. J. Syph.*, 1937, 21, 402.

Excellent results in the treatment of artificially induced malaria. The drug is given intravenously in a dosage of from 0.04 to 0.06 g. every 5 to 7 days. Parasites generally disappeared within 24 hours of the injection, and fever did not recur unless the paroxysm of ague was due within the next 24 hours.—D. Goldman, *Amer. J. med. Sci.*, 1938, 196, 502.

The use of Mapharsen in the treatment of congenital syphilis has much to recommend it. It is safe and easy to administer and reactions are mild and can be completely eliminated with care. An analysis of 40 cases treated over a period of 16 months suggests that the drug is a more powerful agent in affecting a serological cure than any other arsenical compound previously used.—E. A. Morgan, *Canad. med. Ass. J.*, i/1938, 53.

Mapharsen is therapeutically adequate to control infectious syphilis, producing rapid sterilisation of active reactions.—C. R. Rein and F. Wise, *J. Amer. med. Ass.*, ii/1939, 1946.

In all cases of early syphilis the percentage of unsatisfactory results with Mapharside was less than with the arsphenamines. In primary syphilis the contrast is even more significant—the percentage of unsatisfactory results with arsphenamine and neoarsphenamine being more than twice that with Mapharside.—L. Chargin *et al.*, *Arch. Derm. Syph.*, N.Y., 1939, 40, 208.

**Intravenous drip therapy.** At the Mount Sinai Hospital, New York City, neoarsphenamine has now been replaced by Mapharsen. At the present time four doses of the drug in the diluent are given without intermission each day so that the patient receives 240 mg. of Mapharsen in 2400 ml., in 5% dextrose solution, the rate of flow being approximately 3 ml. per minute. The drip is set up at 8 a.m. and the full dose is injected by the end of 10 to 12 hours. At the end of this period the needle is withdrawn, treatment being discontinued during the night and resumed the next morning. This procedure is carried out daily for 5 consecutive days until a total of 1200 mg. of the drug has been administered in 12,000 ml. of diluent containing 600 g. of dextrose. The total arsenic content is approximately 360 mg. The choice of vein is important, the choice of election being a vein on the forearm between the elbow and wrist, the right and left arms being used alternately. With this technique local disturbances are uncommon and infiltrations have occurred in less than 0.5% of cases. Polyneuritis, which

was a troublesome complication with nearsphenamine was reduced to negligible importance in the Mapharsen series.—per *Lancet*, 1/1940, 896.

When nearsphenamine was used approximately one patient in three developed polyneuritis. In addition there was a high percentage of toxic erythema, fever, and reactions referable to the gastro-intestinal tract. Since Mapharsen has been substituted the incidence of reactions has markedly diminished, but (as with nearsphenamine) there have been several cases of hæmorrhagic encephalitis, with two deaths to date.—F. E. Cormia, *Canad. med. Ass. J.*, ii/1940, 184.

## ASAFŒTIDA

*B.P., U.S.P. XI, Fr. Cx., P. Jap. V, P. Helv. V.*

*Dose.*—5 to 15 grains (0.3 to 1 g.). *U.S.P. XI* average dose 6 grains.

An oleo-gum-resin obtained by incision from the root of *Ferula foetida* or other species (*U.S.P. XI* from *F. Assa-foetida* and *F. foetida*). Occurs in greyish-white or yellowish tears, or in masses of agglutinated tears. Nervine stimulant, expectorant and carminative.

**Emulum Asafœtidæ** (*U.S.P. XI*). *Average dose.*— $\frac{1}{2}$  ounce (15 ml.). Asafetida 1 in 25 of distilled water.

**Enema Asafœtidæ** (*B.P.C.*). *Dose.*—4 ounces (120 ml.). Tincture of asafetida 6 to 12% *v/v* in mucilage of starch. For intestinal flatulence.

**Mistura Asafœtidæ Composita** (*St. T. H.*). Asafetida 5 gr., liquid extract of cascara sagrada 10 m., ammonium carbonate 4 gr., infusion of valerian to 1 oz.

**Pilulæ Asafœtidæ** (*B.P.C.*). *Dose.*—1 or 2 pills. Each pill contains 3 grains. If required to be coated should first be coated with acacia mucilage and, when this is dry, with pill varnish. A silver coating may be applied over the varnish, which prevents the silver from being blackened.

**Spiritus Ammoniaë Fetidus** (*B.P.C.*).

*Dose.*—For a single administration, 1 to 1½ drachms (4 to 6 ml.); for repeated administration, 20 to 40 minims (1.2 to 2.5 ml.).

A distilled spirit representing 7½% *w/v* of asafetida with 10% *v/v* of strong solution of ammonia.

**Tinctura Asafœtidæ** (*B.P.*). 1 in 5. *Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

**Galbanum** (*B.P.C., Fr. Cx.*).

*Dose.*—5 to 15 grains (0.3 to 1 g.).

Gum resin from *Ferula galbaniflua* (*Umbelliferae*) and other species. Expectorant and stimulant.

**Pilulæ Galbani Compositæ** (*B.P.C.*). *Syn. PILULÆ ASAFŒTIDÆ COMPOSITÆ.* *Dose.*—1 or 2 pills.

Contain 1 grain each of galbanum, asafetida and myrrh.

**Myrrha** (*B.P., U.S.P. XI, Fr. Cx., P. Jap. V, P. Helv. V.*).

*Dose.*—5 to 15 grains (0.3 to 1 g.).

A yellowish or reddish oleo-gum-resin from *Commiphora molmol* and possibly other species (*Burseraceæ*). **Soluble** in water to the extent of about 50% (forms whitish emulsion on trituration), the remainder being mostly soluble in alcohol 90%. It is soluble in alkalis, *e.g.*, potassium carbonate. A favourite constituent in mouth-washes, *e.g.*, tincture of myrrh and borax.

**Tinctura Myrrhæ** (*B.P.*). *Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.). 1 in 5 of alcohol 90%.

**Tinctura Myrrhæ** (*U.S.P. XI*). *Average dose.*—30 minims (2 ml.). 1 in 5.

**Tinctura Myrrhæ Composita** (B.P.C.). Syn. TINCTURA MYRRHÆ ET ALOES. Myrrh and aloes of each 5% *w/v* in diluted alcohol.

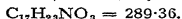
**Tinctura Myrrhæ et Boracis** (B.P.C.). Contains about 33% *v/v* of tincture of myrrh with tincture of krameria, borax and aromatic oils. Used as an astringent mouth-wash and gargle.

### Sagapenum.

**Dose.**—10 to 30 grains (0.6 to 2 g.). A gum-resin, obtained from a species of *Ferula*, with taste resembling that of asafetida, and properties similar to this and galbanum. Has been given in amenorrhœa and hysteria.

## ATROPINA

B.P., Fr. Cx., U.S.P. XI, F.E. VIII.



[P1] "Alkaloids, the following; their salts, simple or complex:—*Atropine*."

[S1] "Alkaloids, the following; their salts, simple or complex:—*Atropine* except substances containing less than 0.15 % of *atropine*."

**Dose.**— $\frac{1}{240}$  to  $\frac{1}{60}$  grain (0.00025 to 0.001 g.). The dose may be increased to  $\frac{1}{15}$ , or in acute mania to  $\frac{1}{2}$  grain or more. Fr. Cx.—**Maximum dose** in 24 hours 0.002 g. It is generally given internally as the sulphate.

Young children are less sensitive to the action of atropine than adults and may require slightly larger doses than those proportional to their weights.

An alkaloid obtained from *Atropa Belladonna*, and other solanaceous plants. Generally in acicular crystals, alkaline in reaction; m.p. 114° to 116°.

**Soluble** 1 in 560 of water, 1 in 50 of boiling water, 1 in 3 of 90% alcohol, 1 in 35 of benzene, 1 in 60 of ether, 1 in 1 of chloroform, 1 in 40 of olive oil; freely soluble in glycerin and oleic acid.

**Incompatible** with caustic alkalis and mercurial salts. Alkalis cause hydrolysis into tropine and alkali tropate. The change takes place when solutions are left in contact with ammonia or alkali carbonates and to some extent with bicarbonates.

The mydriatic alkaloids, atropine and hyoscyamine, may be manufactured from *Atropa Belladonna*, *Datura Stramonium*, and *Hyoscyamus niger*, and hyoscyne may be obtained from the last-named and from *Duboisia Myoppyroides*. Atropine is *dl*-hyoscyamine. It does not exist as such in these plants, but is produced from the *l*-hyoscyamine by careful racemisation with alkali.

**Antidotes.** Give 20 gr. of tannic acid in 4 oz. of water, then empty the stomach by emetic (which may not be effectual) or by a stomach tube (which should be well lubricated because of the dryness of the mucous membrane), using dilute tannic acid solution or a solution of potassium permanganate 60 gr. in 2 gallons of water. Medicinal charcoal, 2 dr. in 4 oz. of water, may

be administered. Keep the patient warm. Give fluids freely to aid excretion. Hot, strong coffee may be given by rectum. Oxygen inhalations and artificial respiration may be necessary. Morphine and pilocarpine are not recommended.

**Uses.** The dominant action of atropine is to depress the nerve-endings of cardiac and unstriated muscles and glands. In addition it first stimulates and then depresses the central nervous system.

By reason of its depressant action on the secretory nerve-endings it lessens secretions, especially the saliva, bronchial secretion, and gastric juice. It is thus used internally to check excessive salivation (*e.g.*, during pregnancy or in mercurial poisoning), to abort incipient catarrh ( $\frac{1}{100}$  gr. of the sulphate in a tumbler of water), and in gastric ulcer. It also lessens the perspiration and is given to check the night-sweats of phthisis and other conditions. Full doses are recommended in the treatment of pulmonary œdema.

By virtue of its depressant action on the vagus, atropine increases the heart rate and is of value in poisoning by morphine, muscarine, pilocarpine, physostigmine, aconitine and the like. It is of value in partial heart-block not due to organic causes, but has no effect in complete heart-block. Excessive vagal stimulation, due to an overdosage of digitalis, may be abolished by means of an injection of atropine. A hypodermic injection of atropine  $\frac{1}{100}$  gr. is usually given, in association with morphine  $\frac{1}{4}$  gr., half an hour before the induction of general anæsthesia to diminish vagal inhibition of the heart and reduce bronchial secretion.

By its action in relaxing spasmodic contractions of involuntary muscle it has been found of considerable value in the treatment of renal and biliary colic, bronchial asthma, whooping cough, urinary incontinence and dysmenorrhœa. In the stomach and intestines, atropine, by lowering the tone of the muscle, abolishes spasmodic contractions which cause colic and griping, and it is commonly prescribed in pills to alleviate the griping associated with the action of purgatives. An injection of atropine sulphate frequently facilitates reduction of a hernia by relaxing intestinal spasm, and intravenous injections have been employed for the gastric crises of tabes.

Injections of atropine, usually combined with strychnine, have been employed in the treatment of alcoholism (*vide infra*), and high-dosage atropine treatment has given remarkable results in the symptomatic treatment of post-encephalitic parkinsonism, in which as much as 54 mg. daily has been given.

Atropine is widely used in ophthalmology as a mydriatic and to paralyse accommodation. Mydriasis (following instillation or lamellæ) occurs in half an hour and lasts for a week or more; accommodation is paralysed in two hours, with recovery in two or three days. It has the disadvantage of increasing intraocular tension, necessitating caution in glaucoma, and its use is contra-indicated in persons over 40. Its prolonged mydriatic action is used in the treatment of iritis to secure rest and to prevent or break down adhesions, and it is also used in interstitial keratitis.



Atropine in aqueous solution is not absorbed by the skin, but when rubbed in with substances which are absorbed, such as alcohol or glycerin, or if applied to mucous membranes or inflamed or broken skin, it paralyses the sensory nerve-endings and acts as a local anæsthetic, and in the form of liniment or plaster is used to relieve the pain of muscular rheumatism, sciatica and gout.

### References to Use of Atropine and its Salts.

**ALCOHOLISM.** 1st week: Injection of atropine  $\frac{1}{160}$  gr., with strychnine  $\frac{1}{80}$  gr., thrice daily; 2nd week: atropine  $\frac{1}{80}$  gr., strychnine  $\frac{1}{80}$  gr., thrice daily; 3rd week:  $\frac{1}{80}$  and  $\frac{1}{80}$  gr. respectively, thrice daily; 4th week:  $\frac{1}{80}$  gr. of atropine without strychnine. Together with a mixture of extract of cinchona, sal volatile, and spirit of chloroform thrice daily.

**GASTRIC ULCER.** For diminishing the secretion of acid in gastric ulcer give  $\frac{1}{160}$  gr. of atropine sulphate in 1 dr. of water before three of the feeds and a double dose the last thing at night. Increase both doses by 10 minims ( $\frac{1}{320}$  gr. of atropine sulphate) every day until the patient complains of dryness of the mouth or paralysis of accommodation. Reduce the doses by 10 minims and continue throughout the period of treatment. The influence of atropine on salivary secretion is approximately parallel to its influence on gastric secretion. It is impossible to guess what will be the adequate dose in an individual.—A. F. Hurst, *Pharm. J.*, ii/1934, 703.

In single maximum doses by hypodermic injection, atropine may have a limited value in reducing secretion and spasm; but in the doses usually employed by mouth, or permissible for any continued treatment, atropine and belladonna are practically without effect on the secretory and motor functions of the stomach.—W. A. Bastedo, *J. Amer. med. Ass.*, i/1936, 88.

In stomach disorders, atropine,  $\frac{1}{80}$  to  $\frac{1}{160}$  gr., in 1 ml. of saline solution intravenously gives relief from nausea, vomiting and pain within from 2 to 5 minutes in patients with smooth muscle spasm secondary to a peptic ulcer or pylorospasm, and in other symptoms thought to be related to the parasympathetic nervous system, including angina pectoris, biliary dyskinesia, ulcerative colitis and the dyspnoea of asthma.—E. A. Lehnher, *J. Amer. med. Ass.*, i/1936, 642.

Atropine should be used only when pain and symptoms suggesting pyloric spasm are present. Its routine administration in the absence of such symptoms is unnecessary because of its failure to influence gastric secretion. When it is given, the small doses usually recommended should be replaced by larger doses, sufficient to produce pharmacological effects, e.g.,  $\frac{1}{80}$  gr. followed by  $\frac{1}{80}$  gr. every four hours until the limit of tolerance is reached.—B. M. Nicol, *Lancet*, ii/1939, 884.

**HYPERTENSION.** Improvement, especially in subjective symptoms, obtained by the oral administration of 0.6 mg. of atropine daily in cases of vascular hypertension. No benefit was obtained in hypertension due to heart disease.—S. Murakami and S. Okinaka, per *Brit. med. J. Epit.*, ii/1936, 15.

**POST-ENCEPHALITIC PARKINSONISM.** Treatment of 16 cases with a dosage of 3 to 5 minims three times a day of a 0.1% solution of atropine sulphate, the dose being increased every day, every other day, or every third day by 1 minim until a single dose contains over 1 mg., when it is given in pill form until an optimum effect is obtained—usually at a dosage of 4 to 8 mg. 3 times a day. Rigidity banished in 6 and diminished in 7 cases, tremor (in 9 cases) disappeared in 1 and diminished in 7. But atropine alone is inadequate; it must be supplemented by such measures as salt-water baths, massage, gymnastics, courses of arsenic and psychic encouragement.—O. J. Nielsen, *Hospitaltidende*, 1935, 806.

**High dosage atropine treatment** causes remarkable improvement in certain cases of post-encephalitic parkinsonism. The greatest benefit is seen in cases in which the disability arises chiefly from muscular stiffness and excessive flow of saliva. Improvement may also occur in tremor, in the frequency of oculogyric attacks and in various spasmodic symptoms. Under no circumstances does the parkinsonian syndrome completely disappear and unless the treatment is maintained and re-enforced by suitable environment, there is usually a rapid return to the pre-existing condition. The dosage begins with 0.5 mg. of atropine daily in the form of 0.5% solution of atropine sulphate given in two doses. This is increased by 0.5 mg. daily, spread over three doses, so long as any objective or

subjective improvement is produced; when this point is reached reduction should be gradual in order to fix the optimal dose on which improvement is maintained. In patients who have previously been for some time on tincture of belladonna, one may give 5 or even 10 mg. of atropine on the first day and increase by 2.5 mg. daily, not only without ill effects but, in suitable cases, with rapid benefit. Up to 54 mg. of atropine daily has been given in this way. After the optimal dose has been reached it is a convenience to prescribe the atropine in coloured tablets, e.g., pink tablets containing 4 mg., yellow only 1 mg. By this combination of strengths it is easy to obtain any required dose, the patient knows exactly how many he has to take of each colour for the required dose, and the coloration distinguishes them from other less potent tablets. There is an occasional rise of temperature during the taking of atropine in large doses, and the possibility of dangerous hyperpyrexia on exposure to heat considerably less than affects normals must not be overlooked.—A. J. Hall, *Brit. med. J.*, i/1937, 796.

**SEASICKNESS.** Tolerance to atropine can be developed by most people if the drug is given in gradually increasing doses. Thus, before long voyages, patients susceptible to seasickness are given atropine as follows: 4 days before embarking 1 mg. is given in 4 doses; the dose is increased by 1 mg. a day so that 4 mg. is taken during the day of departure, and this dosage is maintained throughout the voyage. In patients with pyloric ulcer, a dose as high as 19 mg. a day has been reached.—Danielopolou and Radulesco, per *Lancet*, i/1936, 909.

[P1-S1] **Genatropine** (*Amido Laboratories, Paris; Wilcox, JozEAU, London*). The amino oxide of atropine ( $C_{17}H_{23}O_4N$ ). Supplied in granules containing 0.5 g. (*dose*.—1 or 2 two or three times daily); in 1.5 in 1000 solution (*dose*.—20 drops = 1 mg. of Genatropine, two or three times daily); and in ampoules containing 2 mg. for subcutaneous injection. Therapeutic action and indications similar to atropine, but is much less toxic and is better tolerated.

[P1-S1] **Chloroformum Atropinæ (B.P.C.)**.

1 in 220 in chloroform coloured with alkanna. A rubefacient and anodyne application in neuralgia and rheumatism. Cleaner in use than Chloroformum Belladonnæ.

[P1-S1] **Collodium Atropinæ (B.P.C.)**.

1 in 220 in acetone and acetone collodion. A colourless substitute for belladonna plaster. Allays the irritation of chilblains.

[P1-S1] **Unguentum Atropinæ (B.P.C.)**. 1% in white soft paraffin.

[P1-S1] **Atropinæ Sulphas (B.P., Fr. Cx., P. Helv. V, P. Jap. V, U.S.P. XI, etc.)**. ( $C_{17}H_{23}O_3N$ )<sub>2</sub>.H<sub>2</sub>SO<sub>4</sub>.H<sub>2</sub>O = 694.8. P. Ned. V has 2H<sub>2</sub>O.

*Dose*.— $\frac{1}{80}$  to  $\frac{1}{60}$  grain (0.00025 to 0.001 g.). The dose may be increased to  $\frac{1}{16}$ , or in cases of acute mania  $\frac{1}{8}$  grain. P. Dan. gives  $\frac{1}{80}$  to  $\frac{1}{40}$  grain. U.S.P. XI average dose  $\frac{1}{160}$  grain. Fr. Cx. has maximum dose in 24 hours 0.002 g.; P.G. VI  $\frac{1}{8}$  grain; P. Belg.  $\frac{1}{40}$  grain.

Opaque white minute efflorescent crystals or granules.

**Soluble** 1 in less than 1 of water, 1 in 4 of alcohol 90%; insoluble in chloroform, ether and benzene.

**Incompatible** with bromides, iodides. Quinine hydrochloride is incompatible, but the acid hydrochloride does not precipitate in reasonable dilutions. See also under Atropina.

Atropine sulphate in simple aqueous solution (pH 6.54) may be sterilised at 120° for 20 minutes, but if the reaction is made faintly alkaline (pH 7.3) more than 50% is decomposed by this treatment. Homatropine hydrobromide solutions must not be heated.—S. A. Schou and P. B. Bjerregaard, *Dansk. Tidsskr. Farm.*, 1932, 10, 185.

[P1] **Caapi (Napp, London)**. Tablets each containing atropine sulphate  $\frac{1}{160}$  gr., caffeine 1 gr., phenacetin 2 gr., quinine alkaloid  $\frac{1}{4}$  gr., powdered cinnamon 1 gr. Advocated for the abortion of coryza.

[P1-81] **Glycerinum Atropinæ** (B.P.C., St. T. H.).

Atropine sulphate, 1 in 400, with compound tincture of lavender and glycerin. This is more cleanly than Glycerinum Belladonnæ and does not stain. U.C.H. is similar.

The resinous matter in the compound tincture of lavender deposits. The following keeps better: Atropine sulphate 127½ gr., water 25 oz., spirit of lavender 2 m., spirit of rosemary 2 m., cinnamon oil 1 m., magenta solution q.s., alcohol 90% 1 oz., glycerin to 100 oz.

[P1-81] **Granules de Sulphate d'Atropine** (Fr. Cx.) contain 1 mg.

[P1-81] **Guttæ Atropinæ** (R.L.O.H.). Atropine sulphate 1, 2, 4 or 8 gr. sterilised water to 1 oz.

St. T. H. has 0.5, 1 or 2%; U.C.H. and St. M. H. 0.5 or 1%; W.H. 1%.

[P1-81] **Gutt. Atropin. Dil.** (N.I.F.).

Atropine sulphate ½ gr., distilled water to 2 dr. [D-P1-81] If required with cocaine, add cocaine hydrochloride 1 gr.

Poisoning in a child of five following instillation into each eye of 2 drops of a 1% solution of atropine sulphate. There was restlessness, singing and shouting, and finally convulsions; a scarlatiniform rash developed, with dryness of mouth and dilatation of pupils. Recovery following morphine injections. Review of literature.—C. M. Scally, *Brit. med. J.*, i/1936, 311.

Mental disturbances in a boy of 10 following instillation into each eye of 5 drops of 1% solution of atropine sulphate.—P. J. Duggan, *Brit. med. J.*, i/1937, 918.

[D-P1-81] **Guttæ Atropinæ et Cocainæ** (St. T. H.).

Atropine sulphate 2% and cocaine hydrochloride 2% in sterilised water.

[P1-81] **Guttæ Atropinæ et Quininæ** (Liverpool Eye and Ear Infirmary).

Atropine sulphate 4 gr., quinine sulphate (bisulphate) 4 gr., distilled water 1 oz.

[P1-81] **Lamella Atropinæ** (B.P.).

Contain ⁵⁰⁰⁰⁰ grain (0.000013 g.) of the sulphate in each, for dilating the pupil; others containing [P1-81] ⁵⁰⁰ gr. (R.L.O.H.) paralyse the accommodation. Also prepared containing [D-P1-81] atropine sulphate ⁱ⁰⁰⁰ gr. combined with cocaine hydrochloride ⁱ⁰⁰ gr. and [D-P1-81] cocaine ⁱ⁰⁰ gr. with atropine ⁵⁰⁰⁰ gr. R.L.O.H. has [D-P1-81] atropine ⁱ⁰⁰ gr., cocaine ⁱ⁰⁰ gr.

[P1-81] **Linimentum Atropinæ.**

Atropine 1 (more or less, if ordered), oleic acid 15, castor oil 15, oil of lavender 1, alcohol (90%) q.s. to 100.

In lumbago and other rheumatic affections is very serviceable used with gentle friction; it is readily absorbed.

[P1-81] **Linimentum Atropinæ** (St. T. H.).

Atropine sulphate 38½ gr., compound tincture of lavender 100 m., industrial methylated spirit to 20 oz. A non-staining preparation of the same strength as Lin. Belladonnæ.

[P1-81] **Linimentum Atropinæ et Chloroformi** (St. T. H.).

Liniment of atropine (St. T. H.) 5, chloroform 1.

[P1-81] **Liquor Atropinæ Sulphatis** (B.P.C.).

Dose.—¼ to 1 minim (0.03 to 0.06 ml.), or more.

Strength 1% w/v. Should be freshly prepared.

[P1-81] **Mistura Antidipsomania.**

Dose.—½ ounce (15 ml.).

Concentrated liquors of commerce of cinchona and gentian 10 m., of capsicum ½ m., solution of strychnine nitrate (4 gr. to the oz.) 1 m., of atropine sulphate (1 gr. to the oz.) 1 m., glycerin 1 dr., water to ½ oz. Has been found of great value with strychnine and atropine injections, gradually diminished in strength.

[P1-81] **Oculentum Atropinæ** (B.P.). 0.25% of atropine sulphate in simple eye ointment.

[P1-81] **Unguentum Atropinæ (R.L.O.H.).** Atropine 2, 4 or 8 gr., yellow soft paraffin to 1 oz. Dissolve atropine in chloroform and add to soft paraffin heated to 61°.

[P1] **Oculentum Atropinæ cum Hydrargyri Oxido (B.P.).**

0.125% of atropine sulphate and 1% of yellow mercuric oxide in simple eye ointment. It should be freshly prepared, since the mercuric oxide is very soon acted upon.

[P1-81] **Unguentum Hydrargyri Oxidi Flavi cum Atropina (R.L.O.H.).**

Atropine 2 or 4 gr., freshly precipitated yellow mercuric oxide 4 gr., yellow soft paraffin to 1 oz. Dissolve the atropine in chloroform, mix with the yellow soft paraffin heated to 61° and add the mercuric oxide while cooling.

CORNEAL ULCERS are well treated with an ointment containing atropine and yellow mercuric oxide of each 1%.—P. G. Doyné, *Lancet*, ii/1927, 132.

[D-P1-81] **Oculentum Atropinæ et Cocainæ (B.P.C.).** 0.25% of atropine sulphate and 0.5% of cocaine hydrochloride in simple eye ointment.

[D-P1-81] **Unguentum Atropinæ et Cocainæ (R.L.O.H.).** Atropine 4 gr., cocaine 8 gr., yellow soft paraffin to 1 oz. Proceed as under Unguentum Atropinæ (R.L.O.H.).

[P1] **Oculentum Iodoformi et Atropinæ (B.P.C.).**

5% of iodoform and 0.1% of atropine sulphate in simple eye ointment.

[P1-81] **Unguentum Iodoformi cum Atropina (R.L.O.H.).**

Atropine 2 gr., iodoform 60 gr., yellow soft paraffin to 1 oz. Prepare as Ung. Hyd. Ox. Flav. c. Atropin. (R.L.O.H.).

[P1-81] **Oleum Atropinæ.**

Atropine 1, castor oil *q.s.* to 100. Heat to dissolve (R.L.O.H. 4 grains in 1 ounce). Forms a stable solution.

[P1] **Pessaries of Atropine** are prepared (weight 120 grains) with gelatin mass or at times with oil of theobroma, containing generally  $\frac{1}{20}$  gr. of the alkaloid in each.

[P1-81] **Atropinæ Methylbromidum. Syn. MYDRIASINE.**

$C_{17}H_{23}O_3N, CH_2Br = 384.3$ .

*Dose.*— $\frac{1}{80}$  to  $\frac{1}{40}$  grain (0.001 to 0.002 g.).

An addition product of methyl bromide to the alkaloidal base.

White crystals soluble in water 1 in 1 easily. M.p. about 222°.

*Uses.* Internally similar to those of atropine. Subcutaneously in croupous pneumonia, dry pleurisy and appendicitis; dyspepsia with pyrosis (with sodium bicarbonate), and epilepsy (with bromide). As effect passes off rapidly it is useful in  $\frac{1}{4}$  to 2% solution with cocaine hydrochloride 1% for dilating the pupil in suspected iritis to ascertain whether adhesions exist.

[P1-81] **Atropinæ Methylnitrates. Prop. Name. EUMYDRIN (Bayer Products, London).**  $C_{17}H_{23}O_3N, CH_3NO_2 = 366.4$ .

*Dose.*— $\frac{1}{80}$  to  $\frac{1}{40}$  grain (0.001 to 0.002 g.).

White crystals, soluble in water, obtained by the action of silver nitrate on atropine methylbromide.

A powerful mydriatic, and less poisonous than atropine. 1 or 2% solution dilates the pupil after 25 minutes; the maximum is reached in 50 minutes. Dilatation persists for 12 hours. Also given internally in congenital pyloric stenosis.

CONGENITAL PYLORIC STENOSIS. Eumydrin gives better results than surgery, gastric lavage, or atropine. It is given in the form of a 1 in 10,000 solution (solution does not keep) which is given in a dosage of 5 ml. (= 0.5 mg. per dose) 7 times a day half an hour before feeding; in many cases doses of 0.25 mg. may prove sufficient. The treatment is continued until the patient has not vomited

for a week or more. It is important not to give this treatment as long as the patient is in an extremely dehydrated condition, and not until the introduction of saline has produced satisfactory diuresis.—E. Svensgaard, *Arch. Dis. Childh.*, 1935, 443.

Since the publication of Svensgaard's paper, treatment by Eumydrin has been adopted as the routine treatment in the Children's Hospital of the Leicester Royal Infirmary, and although the results have not been as brilliant as Svensgaard's they compare favourably with those of surgical treatment, and there is reason to believe they will become progressively better. In the few cases in which Eumydrin is not successful it is possible that treatment with some other tropic acid derivative such as Syntropin will succeed.—J. V. Braithwaite, *Brit. med. J.*, i/1938, 334.

Apart from the precaution of overcoming dehydration before Eumydrin is started, there are other important details of treatment if success is to be obtained. If a start is made with 2 ml. it can be increased every second or third day until vomiting is no longer frequent and projectile. The dose ascertained in this way is continued for a few days, after which, if vomiting is still occurring, further increase is required. When vomiting has ceased and while no toxic symptoms are evident, the same dose is continued until the infant has been free from vomiting for 3 to 5 weeks. Subsequently the dose is gradually reduced until finally the drug is stopped. Too early or too rapid withdrawal may result in a return of projectile vomiting.—R. Lightwood, *Practitioner*, ii/1938, 326.

Lately, attention has been drawn to the advantages of an alcoholic solution administered perlingually. One drop of a 0.6% solution is given on the tongue and is stated to be rapidly absorbed. Given in this way none of the drug is lost through vomiting, and the solution remains potent for a considerable time (in the dilute watery solutions the drug soon loses its activity).—*Lancet*, ii/1940, 203.

[P1-81] **Guttæ Methyils Atropinæ Nitratis** (R.L.O.H.). *Syn.* GUTTÆ EUMYDRINÆ. Atropine methylnitrate 2 or 4 gr., sterilised water to 1 oz.

[P1-87] **Asmodrin** (Duncan, Flockhart, Edinburgh). An aqueous solution for the inhalation treatment of asthma, containing atropine methylnitrate, papaverine, sodium nitrate, anterior pituitary, and suprarenal medulla.

[P1-87] **Astevan** (Evans, Sons, Lescher & Webb, Liverpool). An aqueous solution for the inhalation treatment of asthma and hay fever, and containing atropine methylnitrate, papaverine hydrochloride, sodium nitrate, pituitary extract (anterior and middle lobes), adrenaline, chlorbutol and glycerin.

[P1] **Midriverin** (Richter, London). Tablets containing atropine methylnitrate  $\frac{1}{4}$  gr., papaverine  $\frac{1}{2}$  gr. *Dose.*—1 or 2 tablets three times daily. Antispasmodic and in asthma and dysmenorrhœa.

[P1-87] **Nebadrene** (Paines & Byrne, London). Nasal spray containing atropine methylnitrate 0.125%, pilocarpine nitrate 0.1%, papaverine sulphate 1%, adrenaline hydrochloride 0.25%, pituitary (posterior lobe) extract 0.5%, chlorbutol 1.5%, in an aqueous glycerin medium. For bronchial asthma and hay fever.

[P1-81] **Atropinæ Salicylas**.  $C_{17}H_{21}NO_3, C_7H_5O_2 = 427.5$ .

*Dose.*— $\frac{1}{64}$  grain (0.001 g.).

Deliquescent powder or crystals, stated to be superior to the sulphate as more rapid in effect. Soluble 1 in 20 of water.

[P1] **Liquor Atropinæ Salicylatis**. Atropine  $\frac{1}{2}$  gr., salicylic acid  $\frac{1}{2}$  gr., water 1 oz.

**Homatropina**.  $C_{16}H_{21}NO_3 = 275.3$ .

[P1] "Alkaloids, the following; their salts, simple or complex:—Homatropine."

[81] "Alkaloids, the following; their salts, simple or complex:—Homatropine except substances containing less than 0.15% of homatropine."

*Dose.*— $\frac{1}{64}$  to  $\frac{1}{32}$  grain (0.001 to 0.002 g.).

Homatropine is the mandelic acid ester of tropine. In colourless crystals, *insoluble* in water, *soluble* in organic solvents and 1 in 100 of liquid paraffin; also soluble in vegetable oils.

**Uses.** Preferred to atropine as a mydriatic for examining the eye, because its action is more rapid and less prolonged. The effect is exerted in 15 to 30 minutes, and passes off in 6 to 24 hours. Mydriasis is readily controlled by physostigmine. Homatropine is rarely used internally. Large doses may cause, like atropine, staggering gait, and delirium in children. Homatropine slows the heart beats and renders them irregular in force and rhythm.

[P1-81] **Oleum Homatropinæ** (R.L.O.H.).

Homatropine 4 gr., dissolved in minimum quantity of chloroform and mixed with castor oil at 61° to 1 oz.; stir until cold.

[D-P1-81] **Oleum Homatropinæ et Cocainæ** (R.L.O.H.) contains 8 gr. of homatropine and 8 gr. of cocaine per oz. of castor oil. Prepared as the preceding. These oily solutions are not washed out by the tears.

The preparation of a solution in castor oil without the chloroform necessitates warming the alkaloids and oil on a water-bath for several hours.

[P1-81] **Homatropinæ Hydrobromidum** (B.P., U.S.P. XI, P.G. VI, P. Helv. V, etc.).  $C_{16}H_{21}O_3N \cdot HBr = 356.26$ .

**Dose.**— $\frac{1}{81}$  to  $\frac{1}{32}$  grain (0.001 to 0.002 g.). U.S.P. XI average dose  $\frac{1}{120}$  grain.

In minute trimetric crystals; m.p. about 214° (decomp.).

**Soluble** 1 in 6 of water, 1 in 18 of alcohol 90%, and 1 in 133 of dehydrated alcohol; slightly soluble in ether, insoluble in chloroform.

[P1-81] **Lamellæ Homatropinæ** (B.P.) contain  $\frac{1}{100}$  gr. (0.0006 g.) of homatropine hydrobromide.

[P1-81] **Guttæ Homatropinæ** (R.L.O.H.) 4 or 8 gr. of homatropine hydrobromide per oz. of sterile water.

[P1-81] **Gutt. Homatropinæ Dtl.** (N.I.F.). Homatropine hydrobromide  $\frac{1}{2}$  gr., distilled water to 2 fl. dr. [D-P1-81] If required with cocaine, add cocaine hydrochloride 1 gr.

[D-P1-81] **Guttæ Homatropinæ et Cocainæ** (R.L.O.H.). Homatropine hydrobromide 4 or 8 gr., cocaine hydrochloride 8 gr., sterilised water to 1 oz.

[P1-81] **Injectio Homatropinæ Hypodermica**, 1 in 120, is used.

**Dose.**—1 to 6 minims (0.06 to 0.4 ml.).

[P1-81] **Syntropan** (Roche Products, Welwyn Garden City). The phosphate of 3-diethyl-amino-2:2-dimethylpropanol ester of tropic acid. A synthetic antispasmodic. **Dose.**—1 tablet (0.05 g.) 3 or 4 times a day; or by injection 1 ml. (= 0.01 g.) 3 times a day. In all vagotonic states, e.g., vascular tension, coronary spasm, angina pectoris, gastric spasms, dysmenorrhœa.

The relationship between the action of Syntropan and atropine on various organs is found to be very different. While the spasmolytic action of Syntropan, particularly on the intestine, is comparable with that of atropine, it is found that the action on the pupil, on the salivary secretion, and on the vagus is more than 100 to 1000 times less than that of atropine. From this distinct difference of specificity, combined with the lower toxicity observed in man and the shorter duration of the action of Syntropan, it appears possible for the clinician to find therapeutic indications in which Syntropan would have definite advantages over atropine.—K. Fromberg, *J. Pharmacol.*, 1937, 60, 1.

**SEA-SICKNESS.** Tried out with success in twelve cases during a ten weeks voyage to S. America; it gave immediate relief.—Thos. North, *Lancet*, i/1936, 1263.

[P1] **Navigan** (Roche Products, Welwyn Garden City). Tablets for travel sickness containing 10 mg. of Syntropan and 50 mg. of dihydroxydiethylpiperidine, a mild sedative and hypnotic. **Dose.**—3 to 4 tablets at least 30 minutes before going on board, 2 to 3 tablets  $2\frac{1}{2}$  to 3 hours later, preferably 30 minutes before a meal or before retiring, and a third dose of 2 tablets after a further 4 hours. Also available as [P1] **Suppositories** containing 40 mg. of Syntropan and 200 mg. of dihydroxydiethylpiperidine.

[P1-81] **Trasentin** (*Ciba, Horsham*). Diphenylacetyldiethylaminoethanolester hydrochloride,  $(C_6H_5)_2CH \cdot CO \cdot O \cdot CH_2 \cdot CH_2 \cdot N(C_2H_5)_2 \cdot HCl$ , occurring in white crystals readily soluble in water. Has an antispasmodic action similar to that of atropine but without side-effects on the heart, pupil, accommodation, or salivary glands; it resembles papaverine in having a marked action on smooth muscle tissue. The effect is exerted in about 30 minutes after oral or rectal administration and within 10 to 15 minutes of intramuscular injection, complete analgesia being obtained shortly afterwards. Of value in spasms of the gastro-intestinal system, of the urinary passages in lithiasis, and of the biliary ducts, also in dysmenorrhœic spasms. Available in tablets containing  $1\frac{1}{2}$  gr., suppositories containing  $1\frac{1}{2}$  gr. and ampoules of 1.7 ml. containing  $1\frac{1}{2}$  gr. in 1.5 ml. *Dose*.—1 to 2 tablets twice or thrice daily, 1 or 2 suppositories daily, or  $\frac{1}{2}$  to 1 ampoule daily for subcutaneous or intramuscular injection.

## AURANTIUM

**Aurantii Cortex Recens** (*B.P.*) and **Aurantii Cortex Siccatus** (*B.P.*).

The fresh or dried outer part of the pericarp of the ripe or nearly ripe bitter-orange, the fruit of *Citrus Aurantium*.

*U.S.P. XI* includes dried bitter-orange peel and fresh sweet-orange peel. *Fr. Cx.* includes peel, flower and leaf from the bitter orange ("Bigaradier") and peel from the sweet orange ("Oranger Vrai").

**Elixir Simplex** (*B.P.C.*).

*Dose*.—1 to 2 drachms (4 to 8 ml.).

Tincture of orange about 1 in 13 with syrup and distilled water.

**Extractum Aurantii Liquidum** (*B.P.C.*).

*Dose*.—10 to 20 minims (0.6 to 1.2 ml.). About 1 in 1, from dried bitter-orange peel.

**Infusum Aurantii Compositum Concentratum** (*B.P.C.*).

*Dose*.— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Dried bitter-orange peel, 1 in 5, with lemon peel and clove. It is approximately eight times the strength of the fresh infusion.

**Infusum Aurantii Compositum Recens** (*B.P.C.*).

*Dose*.— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.).

Dried bitter-orange peel, 1 in 40, with lemon peel and clove.

**Infusum Aurantii Concentratum** (*B.P.*).

*Dose*.— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.). About 1 in  $2\frac{1}{2}$ . It is approximately eight times the strength of the fresh infusion.

**Infusum Aurantii Recens** (*B.P.*).

*Dose*.— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.). 1 in 20.

**Syrupus Aromaticus** (*B.P.C.*).

*Dose*.— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Liquid extract of orange peel, 1 in 16, with cinnamon water and syrup.

**Syrupus Aurantii** (*B.P.*).

*Dose*.— $\frac{1}{2}$  to 2 drachms (2 to 8 ml.).

Tincture of orange 1, syrup 7.

**Syrupus Aurantii** (*U.S.P. XI*).

Tincture of sweet-orange peel 5, citric acid 0.5, talc 1.5, mixed with water sufficient after filtering to give 45, dissolving sucrose 82 in the filtrate in the cold, and adding water to produce 100.

**Syrupus Citri Aurantii Amari Corticis** (*Fr. Cx.*) is prepared by macerating dried orange peel 100 g., in alcohol 60% 100 g., for 12 hours; adding water heated to 70° 1000 g., filtering after 6 hours and dissolving 180 g. of sugar in every 100 g. of filtrate.

**Tinctura Aurantii (B.P.).**

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

1 of fresh bitter-orange peel in 4 of alcohol 90%. Mixtures containing salts of iron will become dark in colour with all preparations of orange peel.

**Tinctura Aurantii Amari (U.S.P. XI).**

*Average dose.*—60 minims (4 ml.).

Dried bitter-orange peel in 60% alcohol, 1 in 5.

**Tinctura Aurantii Dulcis (U.S.P. XI).**

*Average dose.*—60 minims (4 ml.).

Fresh outer rind grated from sweet-orange peel, in alcohol, 1 in 2.

**Vinum Aurantii (B.P.C.).**

Made by fermentation of a saccharine solution containing fresh bitter-orange peel. It contains 12 to 16% v/v of ethyl alcohol. In practice a boiling 25% sugar solution is poured on to the peel and allowed to stand for 24 hours. Yeast is added and the liquor fermented at 20° for 3 days.

**Oleum Aurantii (B.P.C.).** *Syn.* ESSENCE OF ORANGE, ESSENCE OF PORTUGAL (*Fr. Cx.*).

*Dose.*— $\frac{1}{2}$  to 3 minims (0.03 to 0.2 ml.).

Is obtained by expression of the fresh peel of either the sweet-orange (oil of sweet-orange) or the bitter-orange (oil of bitter-orange), chiefly from the former. The two oils are practically indistinguishable chemically. On keeping, a disagreeable terebinthinate taste develops, stated to be prevented by the addition of 10% of dehydrated alcohol to the freshly distilled oil.

**Terpeneless Oil of Orange** is prepared, being many times (about 65) more potent in flavour and soluble in 60% spirit.

**Elixir Aromaticum (B.P.C.).** *Syn.* ELIXIR AURANTII, ELIXIR AURANTII COMPOSITUM.

*Dose.*— $\frac{1}{2}$  to 2 drachms (2 to 8 ml.).

Contains oils of orange, coriander and anise, in alcohol, syrup and water.

**Elixir Aromaticum (U.S.P. XI).**

Compound spirit of orange 1.2%, with syrup, alcohol and water, and clarified by filtration with 3% of talc.

**Elixir Aurantii Amari (N.F. VI).** *Syn.* ELIXIR OF CURASSAO.

*Dose.*—2 to 4 drachms (8 to 15 ml.).

Oil of bitter-orange 1, tincture of orange 20, alcohol 300, strong orange-flower water 20, syrup 400, distilled water to 1000. Filter through diatomite.

**Spiritus Aurantii Compositus (U.S.P. XI).**

Oils of orange 20%, lemon 5%, coriander 2% and anise 0.5%, in alcohol.

**Oleum Neroli (B.P.C.).** *Syn.* OLEUM AURANTII FLORUM (*Fr. Cx., P. Jap. V.*).

Obtained by distillation from the flowers of the bitter-orange tree. A pale yellow, slightly fluorescent oil, darkening on exposure to air. Is used largely in perfumery.

**Aqua Aurantii Floris (B.P.C., U.S.P. XI, P. Jap. V).** *Syn.* AQUA NAPHÆ (*P. Ned. V, P. Helv. V.*).

The triple water diluted immediately before use with twice its volume of distilled water.

**Aqua Aurantii Floris Concentrata (B.P.C.).**

About 1 in 170 of oil of neroli in diluted alcohol. Is approximately 40 times the strength of orange-flower water.

**Aqua Aurantii Floris Triplex (B.P.C.).**

The undiluted orange-flower water of commerce.



**Syrupus Aurantii Floris (B.P.C.).**

*Dose.*— $\frac{1}{4}$  to 1 drachm (2 to 4 ml.).

Contains 15% *v/v* of the triple water with sucrose and syrup.

**Syrupus Aurantii Florum (U.S.P. XI).**

Orange-flower water 22.5, sucrose 85, water to 100.

**Succus Aurantii (B.P.C.)** is the expressed juice of the sweet-orange, *Citrus sinensis*. It may be concentrated *in vacuo* to one-seventh of its bulk without loss of vitamin C, and is usually supplied commercially as the concentrate.

**Limonis Cortex (B.P.).** The outer part of the fresh pericarp of *Citrus Limonia*.

The dried peel (*Limonis Cortex Siccatus*) is also used occasionally. It has been recommended instead of twice its weight of the fresh peel in making the official compound infusions of gentian.

**Syrupus Limonis (B.P.).**

A mixture of syrup with a solution of citric acid in a strong tincture of lemon peel prepared by maceration in alcohol 60%.

**Syrupus Acidi Citrici (U.S.P. XI).**

Tincture of lemon 1, citric acid 1, water 1, syrup to 100.

**Sirop d'Acide Citrique (Fr. Cx.).** *Syn.* SYRUPUS LIMONIS. Citric acid 10 g., simple syrup 970 g., tincture of lemon 20 g.

**Tinctura Limonis (B.P.).**

*Dose.*— $\frac{1}{4}$  to 1 drachm (2 to 4 ml.).

1 in 4, by maceration with alcohol 60%.

**Tinctura Limonis (U.S.P. XI).**

1 part of the outer grated rind of the fresh fruit macerated with 1½ volumes of alcohol and the residue washed with sufficient alcohol to produce 2 volumes of tincture.

**Oleum Limonis (B.P.).** *Syn.* OLEUM CITRI ÆTHEREUM (*Fr. Cx.*).

*Dose.*—1 to 3 minims (0.06 to 0.2 ml.).

The oil expressed from lemon peel. Contains not less than 4% of aldehydes calculated as citral,  $C_{10}H_{16}O$ .

**Oleum Limonis Deterpenatum (B.P.C.).** *Syn.* TERPENELESS OIL OF LEMON. Is prepared by concentration *in vacuo*, and is both terpene- and sesquiterpene-free. It is about 20 times as strong as oil of lemon.

**Succus Limonis (B.P.C., Fr. Cx.)** is the expressed juice of ripe lemons. It may be preserved with 10% alcohol. It may be concentrated *in vacuo* without loss of vitamin C and is met with in commerce in this form. It contains 7 to 9% of citric acid.

**Syrupus Succo Limonis (B.P.C.).**

*Dose.*— $\frac{1}{4}$  to 1 drachm (2 to 4 ml.).

A lemon syrup prepared with about 50% *v/v* of lemon juice with a tincture of lemon peel added.

**AURUM**

Au = 197.2.

**Auri Bromidum (B.P.C.)** *Syn.* GOLD BROMIDE.

*Dose.*— $\frac{1}{80}$  to  $\frac{1}{2}$  grain (0.001 to 0.012 g.), or up to  $\frac{1}{2}$  grain (0.03 g.).

Consists of potassium bromaurate,  $\text{KAuBr}_4 \cdot 2\text{H}_2\text{O} = 592.0$ , and occurs as a blackish or brown powder or in brownish-red crystals.

**Soluble** 1 in 5 of water and in alcohol.

**Uses.** Has been used in epilepsy, hysteria, migraine, nervous dyspepsia, and whooping cough. Useful in alcoholic neurasthenia combined with hyoscyamine (or atropine) and strychnine.

**WHOOPING COUGH.** Good results obtained from treatment with  $\frac{1}{4}$  gr. of gold bromide for adults and  $\frac{1}{8}$  to  $\frac{1}{4}$  gr. for children, according to age, given as an elixir. Considerable relief was obtained within a few days, and the duration of the illness was greatly decreased. 50 children treated with the usual remedies were sick on the average nearly three times as long as the 100 children receiving gold bromide.—J. Epstein, *Arch. Pediatr.*, N.Y., 1936, 52.

[P1-81] **Liquor Auri et Arseni Brominatus (B.P.C.).** *Syn.* LIQUOR AURI ET ARSENI BROMIDI, LIQUOR AURI BROMIDI ARSENIATUS.

*Dose.*—5 to 10 minims (0.3 to 0.6 ml.).

Contains in 10 m. the equivalent of about  $\frac{1}{4}$  gr. of arsenic trioxide and  $\frac{1}{2}$  gr. of auric bromide.

**Liquor Auri et Hydrargyri Bromidi.**

*Dose.*—5 to 10 minims (0.3 to 0.6 ml.).

Auric bromide, mercuric bromide, of each  $1\frac{1}{2}$  gr., distilled water to 1 oz. Has been used in neurasthenia, epilepsy, syphilis, and acne.

**Auri et Sodii Chloridum (Fr. Cx.).** *Syn.* AURI CHLORIDUM.

*Dose.*— $\frac{1}{10}$  to  $\frac{1}{2}$  grain (0.001 to 0.012 g.), or up to  $\frac{1}{2}$  grain (0.03 g.), in a pill massed with kaolin ointment. Hypodermically,  $\frac{1}{16}$  grain (0.005 g.) has been given.

This consists of sodium chloraurate,  $\text{NaAuCl}_4 \cdot 2\text{H}_2\text{O} = 398.1$ , known commercially as "chloride of gold," and containing about 50% of Au. It is an orange-yellow crystalline powder, **soluble** 1 in 2 of water, only partially soluble in alcohol.

**Incompatible** with organic compounds and reducing agents.

It is sometimes used as a caustic, and has been given internally for cirrhosis of the kidney. Pills containing  $\frac{1}{10}$  gr. have been found to retard the development of locomotor ataxia, given preferably in monthly courses alternating with arsenic. Combined with strychnine it is useful in neurosis.

Eye affections associated with leprosy, such as conjunctivitis and iridocyclitis, have been treated with this chloride of gold in  $\frac{1}{10}$  gr. doses given intravenously at 10-day intervals for 2 to 4 injections.

**LUPUS ERYTHEMATOSUS** treated by gold salts intravenously. Of the chloride, 1 ml. of 0.1% once a month, increased to 5 ml. and if necessary to 10 ml. Results fully equal to those from complex compounds. The latter had annoying sequelae not seen with gold chloride. The 0.1% is strongly bactericidal and does not need boiling.—*Brit. med. J. Epit.*, ii/1930, 46.

[P1-81] **Dipsomania Tablets (Parke, Davis, London).** Contain gold and sodium chloride  $\frac{1}{4}$  gr., strychnine nitrate  $\frac{1}{10}$  gr., nitroglycerin  $\frac{1}{100}$  gr., atropine  $\frac{1}{100}$  gr., tinct. digitalis 3 m., oleoresin of capsicum  $\frac{1}{2}$  m. *Dose.*—1 to 2 tablets.

[P1-81] **Auri et Potassii Cyanidum.**  $\text{KAu(CN)}_2 \cdot 2\text{H}_2\text{O} = 324.3$ .

*Dose.*— $\frac{1}{10}$  to  $\frac{1}{2}$  grain (0.001 to 0.02 g.)—with caution.

White crystalline soluble powder.

Has been used in lupus and in syphilis. *Intravenously* the dose was found to be 0.02 to 0.05 g. for adults, and 0.0005 to 0.03 g. for children. To the dose in 1% solution, 50 ml. of normal saline solution are added, and given every second or third day to the extent of 12 injections. The injection is said to be quite painless. After 48 hours a local reaction occurs.

**Auri et Sodii Thiosulphas** (B.P.C.). *Syn. and Prop. Names.* AUROBIN (*Richter, London*), NOVACRYSIN (*Napp, London*), CRISALBINE (*Pharmaceutical Specialities (May & Baker) Ltd., London*), SODIUM AUROTHIOSULPHATE.  $\text{Na}_3\text{Au}(\text{S}_2\text{O}_3)_2 \cdot 2\text{H}_2\text{O} = 526.5$ .

(A foreign proprietary of similar composition was formerly issued under the Registered Trade Name SANOCRYSIN.)

**Dose.**— $\frac{2}{3}$  to 15 grains (0.025 to 1 g.). *Intravenously* initially 0.01 g., gradually increasing, if tolerated and no violent reaction, to 0.015 g. per kilo weight *i.e.*, a maximum of 1 g. per average adult's weight of 10 stone. Solutions must not exceed 5% strength. May also be given *intramuscularly* if intravenous method is inconvenient, *e.g.*, in children. In this case a 3% aqueous solution is used, or a 5 to 10% suspension in oil.

A double thiosulphate of gold and sodium occurring in colourless, odourless stable crystals with a sweet taste. Contains about 37% of Au.

*Soluble* very readily in water, insoluble in alcohol.

**Toxic Reactions.** These are typical of metallic poisoning, and consist of fever, diarrhoea and vomiting with albuminuria and skin reactions of various kinds. In severe cases there may be aplastic anaemia and, rarely, agranulocytosis. Treatment is by sodium thiosulphate, orally or by injection. Mild skin reactions such as localised rashes or papular eruptions usually yield to a few doses of sodium thiosulphate 10 gr. given thrice daily. No patient who has had the treatment should be exposed to bright sunlight, as it may result in lilac-coloured pigmentation of the parts exposed.

The reactions provoked by gold therapy may be prevented or checked by giving large doses (three or four times that usually considered the normal demand) of vitamins A, B<sub>1</sub>, B<sub>2</sub> and C before and during treatment.—K. Secher, *Lancet*, i/1938, 996.

**Uses.** Introduced for the treatment of tuberculosis by H. Moellgaard, of Copenhagen, and, although found to have no bacterial action on tubercle bacilli *in vitro*, is of value, particularly in early exudative cases and as an adjunct to collapse therapy in bilateral cases. The chief contraindications to its use are diarrhoea, nephritis, eczema, cachexia and dense fibrosis. If an injection causes a severe febrile reaction the dose must be reduced.

Its most successful employment is in the treatment of lupus erythematosus; marked improvement or entire healing of the lesion occurs in about two-thirds of the patients, but it must be used with great care and in small dosage in the disseminate type. It has also been used with considerable success in rheumatoid arthritis, preferably administered intramuscularly in oily suspension in doses of 0.1 g., increased by 0.05 to 0.1 g. at intervals of two or three days. Toxic effects are frequent, however, and cases should be carefully selected. The blood sedimentation rate is a useful guide as to the suitability of the case (*see* Vol. II).

**LUPUS ERYTHEMATOSUS.** In 30 cases there were 27 clinical cures and improvement in the remainder. **Dose.**—0.025 g. in 2 ml. water once weekly intravenously, increased by 0.005 g. weekly, provided there are no toxic

symptoms, up to a maximum of 0.1 g.—A. J. Markley and O. S. Philpott, *J. Amer. med. Ass.*, ii/1929, 235.

Of 31 cases treated, 20 (64.5%) were cured. Dosage began with 0.05 to 0.1 g., a dose of 0.25 g. being seldom exceeded. Courses of 8 weekly injections followed by a month or two's rest. Toxic reactions in 18 cases.—J. L. Franklin, *Brit. J. Dermat.*, 1934, 66.

Of 76 cases treated 37% were cured, 34% almost cured or greatly improved, 13% improved slightly and 12% failed to respond favourably. The amount required for a cure varied from a minimum of 12 mg. in one patient to 2750 mg. in another. 24% of cases suffered a reaction of one type or another, the commonest being a scarlatiniform dermatitis. In subacute or quiescent cases initial dose 25 mg., second dose 50 mg., and subsequent doses 100 mg., at weekly intervals. In acute cases initial dose should not exceed 5 mg. In a few cases the dose was increased to 200 or even 300 mg.—C. S. Wright, *Arch. Derm. Syph., N.Y.*, 1936, 413.

**RHEUMATOID ARTHRITIS.** Gold treatment has been used for four years in 900 cases of arthritis; 750 were examples of rheumatoid arthritis. Apparent cure or striking improvement occurred in 80% of the cases of rheumatoid arthritis. Relapse may occur, especially after the first course, but if treatment is continued a second relapse is rare. All patients should have at least two full courses. Toxic reactions occurred in 40% of cases, but as a rule did not contraindicate further treatment. Gold treatment is of doubtful value in other forms of arthritis.—S. J. Hartfall, H. G. Garland and W. Goldie, *Lancet*, ii/1937, 838.

**TUBERCULOSIS.** About 50% of tuberculous patients having a stationary or downward progressive advanced tuberculosis of the "B" or "C" types, when given Sanocrysin in well-regulated doses, will show (1) a rather prompt cessation of symptoms, the changes tending to be permanent if the patient observes the usual measures of hygiene; (2) a clearing of tuberculous infiltration, with marked fibrosis and contraction of cavities; and (3) changes from unfavourable to favourable laboratory findings. Of the remainder, about a third show a temporary improvement for a few weeks or months, while the others show no favourable change or prove incapable of tolerating the drug at all. Gold therapy may often shorten the convalescent period, prolong life, or both. As to selection of cases, it does not seem a matter of duration or stage of disease, so long as the disease is not overwhelming and there are relatively recent discrete tubercles, all of which mean "reactability" on the part of the patient. The intravenous injection of gold salts should not be done shortly after a meal; and it is not enough to receive the assurance of the patient that the bowels are regular.—K. J. Henrichsen and H. C. Sweany, *Amer. Rev. Tuberc. (Suppl.)*, Oct., 1933, 28.

In a total of 1418 cases of pulmonary tuberculosis treated between 1928 and 1933, 60.6% were ameliorated. Gold, in any form yet known, cannot be accepted as a specific treatment—it is inconstant and irregular in its results and there is disparity of effect between one patient and another and even in the same patient at different times. At the same time it is a valuable treatment when carefully employed by experienced physicians. For the avoidance of untoward reactions it is important that the gold salts should be dissolved in a solution of calcium gluconate. It is unnecessary and unwise to stop the treatment after a total of 5 or 6 g. has been given: the amount may be increased up to a total of 20 or 30 g., advancing with small doses spaced at intervals of one week.—L. Bernard and C. Mayer, *Bull. Soc. méd. Hôp. Paris*, 1934, 50, 1168.

#### OTHER PROPRIETARY GOLD COMPOUNDS

**Allochrysin** (*Lumière, Lyons; Anglo-French Drug. Co., London*). Sodium aurothiopropionalsulphonate,  $\text{CH}_3\text{SAu}\cdot\text{CHOH}\cdot\text{CH}_2\text{SO}_3\text{Na}$ , containing 35% of gold, issued in concentrated solution containing in 2 ml. 0.2, 0.1 or 0.05 g., together with ampoules containing 8 ml. of saline diluent.

For use in all developing cases of rheumatoid arthritis or infective periarthritis. Also used in tuberculosis and other indications for chrysotherapy (*vide* Auri et Sodii Thiosulphas).

**Dose.**—A series of 3 intramuscular injections of 0.05 g. at 5-day intervals, followed (if no reaction) by weekly injections of 0.1 g. to a total of 1.5 or 2 g., then a rest of 6 or 8 weeks followed by a second series with the same rest interval at the end. Then continue by subsequent series of 10 to 20 weekly injections of 0.1 or 0.05 g. for a year or two.

**RHEUMATOID ARTHRITIS.** Good results obtained with gold salts, the salts employed being aurothiopropionol sulphonate of sodium, thiosulphate of gold and

sodium, thiomalate of gold and sodium, aurothioglucose and aurothioglycolate of calcium. With small doses at regular intervals and proper selection of cases severe reactions rare. In 500 cases followed up during periods of 2 to 5 years, early cases of under 2 years' duration were cured in the proportion of 50%, the remainder being greatly improved; cases of older standing improved in 80% and cured in 20 to 30%.—Jacques Forestier (Aix-les-Bains), *Brit. med. J.*, i/1934, 350.

100 cases of chronic arthritis treated over a period of 5 years with various gold preparations—Allochrysine, Crisalbine, Myocrisin—12 cases cured, 38 very much improved, 38 improved, and 12 not improved. Few cases escape toxic signs or symptoms, though in the great majority they are slight.—H. S. Pemberton, *Lancet*, i/1935, 1037.

Severe reactions may be avoided by mixing the Allochrysine injection of 0.1 g. (given intramuscularly) with 10 ml. of 10% calcium gluconate.—H. J. Williams, *Brit. med. J.*, ii/1935, 1098. See also H. Roche, *ibid.*, i/1936, 31.

**Lopion** (Bayer Products, London) ("G.2949"). The sodium salt of aurothiosinamine benzoic acid. A water-soluble compound containing about 40% of gold.

*Dose.*—Initially intravenously 0.01 g.; routine, 0.1 increasing to 0.5 g.

The gold is concentrated in the liver instead of in the kidneys. Said to be 10 times less toxic than Krysolgan. Indications as for gold and sodium thio-sulphate. In fresh or extensive disease smaller doses must be employed.

**Myocrisin** (Pharmaceutical Specialities (May & Baker) Ltd., London).

Sodium aurothiomalate in aqueous solution or oil suspension for intramuscular injection in tuberculosis, rheumatoid arthritis and lupus erythematosus, etc. Available in dry ampoules in various doses from 0.01 to 0.5 g. In rheumatoid arthritis an initial dose of 0.01 g. may be followed at weekly intervals by gradually increasing doses until a maximum dose of 0.2 g. is reached, which is continued until a total of 1.5 to 2 g. has been given.

**Neo-Solganal** (Schering, London). Calcium gold keratinate for intramuscular injection (in a series of seven graded doses ranging from 0.01 to 1.0 g.) in rheumatoid arthritis, lobar pneumonia, tuberculosis, lupus erythematosus, etc.

**Parmanil** (Bayer Products, London). A 2 or 5% oily suspension of a methyl-glucamide of aurothioglycollic acid, a water-soluble compound containing 50% Au advocated for intramuscular injection in rheumatoid arthritis, also in tuberculosis, lupus erythematosus, leprosy and lymphogranuloma inguinale.

*Dose.*—The average dose in rheumatoid arthritis is 4 injections of 0.5 ml. of 5% solution, then 2 doses each of 0.75, 1.0, 1.25, and 2 ml., the injections being given weekly.

**RHEUMATOID ARTHRITIS.** Results in 50 cases treated over one year show that the effects of small doses of Parmanil are as good as, or better than, those obtained with large doses of any other gold salt (comparison with 690 cases). Toxic reactions occurred in one-quarter of the cases. Parmanil is one of the least toxic of gold salts. It is given intramuscularly starting with 0.5 ml. of the 5% suspension (0.025 g.) gradually increased up to 2 ml. (0.1 g.). A course usually consists of 12 weekly injections. Of the 50 cases treated, 19 had two courses of injections and 31 one course.—S. J. Hartfall, *Lancet*, ii/1938, 1410.

**Solganal** (Schering, London).

The di-sodium salt of 4-sulphomethylamino-2-auromeraptobenzol-1-sulphonic acid,  $C_7H_5O_4N_2Na_2Au$ . An organic compound of gold for intravenous injection for the treatment of tuberculosis, streptococcal infections, multiple sclerosis, infective arthritis, lupus erythematosus and psoriasis. Has also been used in leprosy. Available in dry ampoules, in conjunction with ampoules of solvent, in various doses from 0.01 to 1 g.

**Solganal B** and **Solganal B Oleosum** are, respectively, a solution and an oily suspension of aurothioglucose,  $C_7H_7O_4SAu$ , an organic compound of gold, for intramuscular injection. Used for the same purposes as the preceding.

**Solganal Dragées** are prepared containing 0.01 g. and 0.1 g. of Solganal for oral administration in the treatment of infective arthritis. *Dose.*—0.01 g. per day, increased by 0.01 g. each day until 0.1 g. is reached, then given on alternate days, each dose being increased by 0.1 g. to a maximum of 0.6 g. Total to be given in a course, 6 to 8 g.

Treatment of arthritis and rheumatism with Solganal B Oleosum intra-muscularly. Of no great value in acute and sub-acute rheumatism in children

and contraindicated where severe carditis is present, but superior to other methods in rheumatoid arthritis.—G. Slot and co-workers, *Lancet*, i/1934, 73.

It is not claimed that gold is a specific for every case of arthritis but there is no doubt that in certain groups of cases results are being obtained which are not secured by other means. The usual technique is to give a course not exceeding 1.5 g., at weekly intervals, of Oleosancrysine, or Solganal B, then a month's holiday, then a second course, then 2 months' holiday, and then a third course. Reactions occur, especially a rash, but with small doses of gold serious results do not seem to occur. Collosol sulphur is used as an adjuvant. Description of 5 cases (osteo-arthritis and rheumatoid arthritis), resistant to other treatment, successfully treated.—G. Slot, *Proc. R. Soc. Med.*, Jan., 1936, 224.

As a result of the use of gold treatment (Crisalbine, Solganal B Oleosum, and Lopion) in 374 cases of rheumatoid arthritis, cure or marked improvement occurred in 78%, and slight improvement in a further 15%. Reduction in dosage followed by reduction in toxic reaction without sacrificing therapeutic effects. Maximum single dose should not exceed 0.1 g. and total for each course not more than 1.0 g., with at least two courses at an interval of not less than three months. Chrysotherapy the most important form of treatment for rheumatoid arthritis.—S. J. Hartfall and H. G. Garland, *Lancet*, i/1936, 1459.

Chrysotherapy should only be undertaken when the case is severe enough to warrant such a very real risk (of accident), which should be explained to the patient before treatment is instituted.—G. J. V. Crosby, *Lancet*, i/1936, 1463.

**Triphal** (Bayer Products, London). Sodium salt of aurothiobenzimidazole-carboxylic acid. Given in doses of 0.025 to 0.2 g. in tuberculosis.

### Colloidal Gold.

Colloidal gold solution may be prepared by the following method:—Neutralise a gold and sodium chloride solution with dilute sodium carbonate solution and adjust the strength to 0.05% Au. With 10 parts of this solution mix 10 parts of a solution containing the calculated amount of formaldehyde required to reduce the gold, reckoning  $3\text{H}\cdot\text{COH}$  to 2 molecules of the gold compound. Employ gelatin as protective. Warm to effect reduction. It can be boiled to sterilise. The finished red hydrosol is to contain 0.025% (1 in 4000) of gold and the same amount of protective.

**Dose.**—1 to 5 millilitres, 0.00025 to 0.00125 g. or  $\frac{1}{8000}$  to  $\frac{1}{4000}$  gr. approx. of gold, intramuscularly or intravenously. More may be given.

**Uses.** Has been used in the treatment of neurasthenia, alcoholism and morphine addiction. In epilepsy, alcoholic neurasthenia and migraine it has been given hypodermically four times daily (usually 2 ml. divided over the day, but this may be increased) with bitter tonics and digestives, every two hours, *per os*.

**Oragol** (Anglo-French Drug. Co., London). Ampoules of solution of colloidal gold (0.01%) and colloidal silver (0.09%) for intramuscular or intravenous injection. Used in bronchitis, endocarditis and acute articular rheumatism, and also, if used early, for cutting short an attack of pneumonia, influenza or erysipelas.

## AZORUBRUM

(and other medicinal dyes)

**Azorubrum** (B.P.C.). *Syn.* BORDEAUX B.

$\text{C}_{20}\text{H}_{12}\text{N}_2\text{O}_7\text{S}_2\text{Na}_2 = 502.2$ . Colour Index No. 88.

The sodium salt of  $\alpha$ -naphthaleneazo- $\beta$ -naphthol-3 : 6-disulphonic acid, occurring as a brown powder *soluble* in water and in alcohol.

**Liquor Azorubri (B.P.C.).** *Syn.* LIQUOR RUBER. 1% w/v in glycerin and chloroform water.

Used as a colouring agent for medicines, 5 m. per oz. usually being sufficient.

From a comprehensive review of 32 selected dyestuffs examined in detail, a general impression was gained that whilst Bordeaux B may be considered to be the most suitable all-round dyestuff for colouring pharmaceuticals, it is often possible in any particular case to find a dyestuff better suited to that particular preparation. It is suggested that more than one red dyestuff should be made officially available, the most suitable being acid magenta (Colour Index 692), amaranth (C.I. 184), Bordeaux B (C.I. 88) and lissamin red 6BS (C.I. 57). An improved formula for solution of Bordeaux B is given, and the paper also includes a scheme for the extraction and identification of dyestuffs.—C. L. M. Brown, *Quart. J. Pharm.*, 1939, 332.

**Amaranth.** *Syn.* BORDEAUX S. Colour Index No. 184.

The sodium salt of 4-sulpho- $\alpha$ -naphthaleneazo- $\beta$ -naphthol-3:6-disulphonic acid. It is soluble in water, but sparingly soluble in alcohol.

Recommended as a colouring agent for medicines, and in some cases found to be preferable to Bordeaux B.

**Congo Red.** *Syn.* SODIUM DIPHENYLBISAZOBISNAPHTHYLAMINE-4-SULPHONATE.

*Dose.*—0.25 ml. of 1% solution per kg. body weight, by intravenous injection. Solutions should be prepared by adding the powder to sterile water, heating if necessary; they should be used as soon as possible after preparation since the dye hydrolyses slowly in solution.

A reddish-brown powder *soluble* in water. Administered intravenously in the treatment of hæmoptysis and as a diagnostic agent for amyloid disease. Amyloid tissue is readily stained by the dye and the proportion in the blood plasma rapidly falls.

In connection with clinical injections of congo red, only the purest brands of the dye should be employed, and the possibility of a thromboplastic effect should be borne in mind in the case of each patient.—D. I. Macht *et al.*, *J. Amer. pharm. Ass.*, 1939, 495.

RIGORS avoided by using Grubler's congo red (*Agents: Baird and Tatlock, London*), which is free from impurities, made up in freshly prepared solution.—J. E. Wallace, *Brit. med. J.*, ii/1934, 881. Preparation of solution with triple-distilled water and filtration through glass wool an important factor in prevention of rigor.—J. Libman, *ibid.*, 882.

**Congo Red** (biologically tested) (*British Drug Houses, London*) is a specially purified form for intravenous administration.

**AMYLOIDOSIS, DIAGNOSIS OF.** A comparatively accurate method for the diagnosis of amyloid disease is by intravenous injection of 0.25 ml. per kg. of a freshly prepared sterilised 1% solution of Grubler's congo red, the percentage decrease of the dye content of the plasma or serum over a period of one hour being estimated colorimetrically. In normal persons 10 to 30% disappears and in amyloid disease anything between 30 and 100%. Technique described.—J. E. Wallace, *Lancet*, i/1932, 391.

**HÆMOPTYSIS.** 5 to 10 ml. of a 1% solution of congo red intravenously is a satisfactory hæmostatic.—A. J. Scott Pinchin and H. V. Morlock, *Prescriber*, ii/1933, 389.

Intravenously of value in hæmoptysis, the dose being 10 ml. of a 1% solution, repeated if necessary in 4 to 6 hours. The injection is often followed by a rigor of short duration which never gives cause for alarm. Congo red produces an increase in the monocytes, an increase in blood platelets, an increase in blood

fibrin content, and a reduction in clotting time.—H. V. Morlock and A. J. Scott Pinchin, *Brit. med. J.*, ii/1934, 783.

Treatment successful in 49 out of 58 cases of tuberculous hæmoptysis.—H. Diaz, per *J. Amer. med. Ass.*, ii/1935, 1228.

**HÆMORRHAGE.** Intravenous injection of 5 or 10 ml. of congo red is a valuable adjunct in the treatment of hæmorrhage from the urinary tract, e.g., in renal injury, bilateral renal and ureteral calculi, chronic pyelonephritis, vesical calculus, tumour of the bladder, urethral trauma, etc. No untoward effects have followed its use. It has also been employed with marked success in severe epistaxis and hæmorrhage after tooth extraction.—R. C. Graves and C. J. E. Kickham, *New Engl. J. Med.*, 1936, 214, 782.

**Indicarminum (B.P.).** *Syn.* INDIGO CARMINE, SODIUM INDIGOTINDISULPHONATE (*Fr. Cx.*).  $C_{16}H_8O_8N_2S_2Na_2 = 466.2$ .

*Dose.*—By intramuscular injection,  $\frac{1}{2}$  to  $1\frac{1}{2}$  grains (0.05 to 0.1 g.); by intravenous injection  $\frac{1}{2}$  to  $\frac{1}{4}$  grain (0.008 to 0.016 g.).

The disodium salt of indigotin-5 : 5'-disulphonic acid, occurring as an odourless blue powder with a coppery lustre.

*Soluble* about 1 in 100 of water; almost insoluble in alcohol 90%. Used as a test for renal efficiency.—*See* Vol. II.

**Magenta (B.P.C.).** *Syn.* FUCHSINE, BASIC FUCHSINE, ROSANILINE HYDROCHLORIDE, ANILINE RED, RUBINE. Colour Index No. 677.

*Dose.*— $\frac{1}{2}$  to 4 grains (0.03 to 0.25 g.), in a pill.

Iridescent crystals consisting of a mixture of pararosaniline (Colour Index No. 676) (hydrochloride of triaminotriphenylcarbinol anhydride) and rosaniline (hydrochloride of triaminodiphenyltolylcarbinol anhydride).

*Soluble* in water, and 1 in 8 of alcohol 90%.

The aqueous solution is used as a colouring agent and, as carbol-fuchsin, as a stain for *B. tuberculosis* (*vide* Clinical and Bacteriological Notes, Vol. II).

**Unguentum Fuchsin** 5% in soft paraffin. Has been used in carbuncle and soft chancre. Also useful for impetigo.

[P2] **Pigmentum Carbol-Fuchsin** (*St. T.H.*).

Basic fuchsin (saturated solution) 10 ml., phenol 5 g., boric acid 1 g., resorcinol 10 g., distilled water 100 ml. Dissolve the phenol in the fuchsin solution, filter and add the boric acid. Stand two hours and finally add the resorcinol.

**Fuchsin Paint** (*Castellani*).

Epidermophytosis of the toes (Mango toe) and other forms of epidermophytosis well treated with a paint consisting of saturated alcoholic solution of basic fuchsin 10 ml., 5% phenol solution 100 ml. Filter and add boric acid 1 g.; after 2 hours add acetone 5 ml.; 2 hours later add resorcinol 10 g. Keep in dark-coloured stoppered bottles. Should be employed initially with care and in small amount.—A. Castellani, *Lancet*, ii/1928, 596.

Carbol-fuchsin paint, with 2.5% of salicylic acid added, the best treatment for epidermophytosis. Rub the *nails* thoroughly with the paint twice daily, even after the disease seems to have subsided. Three months' treatment is required for a cure.—J. Hasson, *Brit. med. J.*, ii/1934, 928.

**PRURITUS ANI.** Many patients obtained dramatic relief from the application of this paint, though without exception these patients all had typical "athlete's foot."—C. N. Morgan, *Practitioner*, ii/1939, 522.

**Acid Fuchesine** (Colour Index No. 692) is a mixture of the sodium or ammonium salts of di- and tri-sulphonic acids of magenta. Soluble in water and alcohol 90%.

**Rosaniline** (*Syn.* ROSEINE) Acetate.  $C_{20}H_{12}N_2 \cdot C_2H_3O_2 \cdot 5H_2O = 451.3$ .

Dark red crystals soluble in water and in alcohol. Both this compound and magenta are sometimes called "roseine."



**Methylviola** (*B.P.C.*, *P. Helv. V*, *P. Jap. V*). *Syn.* METHYL VIOLET, METHYL ROSANILINE, PYOKTANIN. Colour Index No. 680.

In green crystalline powder consisting of a mixture of the hydrochlorides of principally tetra-, penta-, and hexamethylpararosanilines. There are numerous methyl violets, the particular shade depending on the degree of methylation.

**Soluble** 1 in 20 of water, 1 in 20 of alcohol 90%, 1 in 16 of glycerin, and in oleic acid. Insoluble in liquid paraffin.

Dilute solutions have been injected locally and applied for malignant growths, but crystal violet, a purified methyl violet, is now generally used.

**Viola Crystallina** (*B.P.C.*). *Syn.* CRYSTAL VIOLET, METHYL-ROSANILINE, MEDICINAL GENTIAN VIOLET (*vide infra*), HEXAMETHYLPARAROSANILINE HYDROCHLORIDE. Colour Index No. 681.

**Dose.**—0.003 to 0.007 gramme per kilo body weight (=3 to 7 grains for a 10-stone man) intravenously in a  $\frac{1}{4}$  to 1% aqueous solution.

**GENTIAN VIOLET.** According to the Colour Index, commercial gentian violet, as supplied in Gt. Britain, is a mixture of methyl violet and dextrin. For medicinal purposes it should be free from dextrin and in *N.N.R.* Gentian Violet Medicinal is described as a mixture of penta- and hexamethylpararosaniline chlorides. Since the tetra-, penta- and hexa-compounds show no appreciable difference in therapeutic effect, while the hexa-compound, crystal violet, is most readily obtained pure, the latter is usually intended when gentian violet is required in medicine.

Greenish-bronze crystals or powder.

**Soluble** 1 in 20 of water, 1 in 16 of glycerin, 1 in 20 of alcohol 90%. The dye is precipitated from aqueous solution by sodium chloride and other electrolytes.

**Uses.** A powerful antiseptic with selective action on gram-positive organisms. It has been employed intravenously in staphylococcal septicæmia and endocarditis and has been tried in encephalitis.

For *direct application* a solution 1-1000 to 1-500 has been recommended; for instillation 1-10,000, and for *intravenous injection* 5 mg. per kilo-weight, injected in 0.5% solution.

Encouraging results have been obtained in acute infections of joints by lavage and direct medication. Also in post-influenzal empyema by intrapleural instillation of 1-10,000 to 1-1000 solutions.

A 1% aqueous solution, employed either alone in the form of a spray or as a jelly, or in association with tannic acid (*q.v.*), has been found valuable in the treatment of burns, and a 2% solution gives good results in chronic leg ulcers and mycotic skin affections.

Given internally in the form of enteric-coated pills or tablets, it is stated to be a specific for Strongyloides infestation. It is given in a dose of  $2\frac{1}{2}$  grains thrice daily after meals for ten days.

**BLEPHARITIS.** An effective method of treatment of chronic blepharitis of the squamous type in children consists in the application of the following paste ("Blue Compound") by means of a soft camel-hair brush to the roots of the eyelashes after the crusts have been removed with boric lotion:—gentian violet  $\frac{1}{2}\%$ , brilliant green  $\frac{1}{2}\%$ , wool fat to 100. The paste colours the skin temporarily but is easily washed off. It is applied twice daily morning and evening. All squamous cases were free of symptoms in eight weeks, but ulcerative cases showed little or no improvement.—A. T. Elder, *Brit. med. J.*, ii/1940, 185.

**BURNS.** A 1% solution gives excellent results. Without preliminary cleaning of burned area the dye is sprayed on at 2-hour intervals for the first few hours. No dressing applied but surface exposed to air and protected by a cradle. An eschar is rapidly formed and spraying is then performed every 4 to 6 hours during the day till healing is complete. Analgesia almost instantaneous.—*Lancet*, i/1933, 484.

A jelly prepared by the addition of 30 g. of tragacanth to 1000 ml. of 1% solution gives superior results to an aqueous solution in the treatment of burns.—J. H. Connell, *J. Amer. med. Ass.*, i/1933, 1220.

For extensive burns the following treatment closely approaches the ideal. After washing the burnt areas with tincture of soft soap, open blisters and remove loose skin. Then spray the burn with a 1% aqueous solution of gentian violet (methyl-rosaniline) and after a few minutes swab the entire area with 10% silver nitrate. The patient is then placed in a tent at 85° to 90°F. and the area resprayed with gentian violet every 15 minutes for about five times; after that the spray is applied once or twice every day. Fluids are forced by mouth, and saline solution given by hypodermoclysis as indicated by the patient's condition. The patient is moved about as soon as the crust is established and allowed to walk about when the period of shock is over.—H. E. Branch, *Ann. Surg.*, 1937, 35, 478.

Sepsis in burns usually begins in areas of the (tannic acid) coagulum which have cracked or become moist; to prevent these defects, the area is dehydrated with ether every four hours and then painted with 1% solution of gentian violet in spirit. Should the coagulum become moist, ether and gentian violet are applied more frequently.—W. M. Dennison, *Lancet*, ii/1939, 1108.

The following jelly is recommended in place of tannic acid jelly for the treatment of burns on the fingers and hands:—gentian violet (or methyl violet) 1%, quinine and urea hydrochloride 0.5% in a glycerin-tragacanth base (powdered tragacanth 2%, glycerin 10%, water to 100).—J. F. Heggie and R. M. Heggie, *Lancet*, ii/1940, 391.

In the Navy and R.A.F. a jelly containing gentian violet 1%, merthiolate 1 in 5000, has now been substituted for tannic acid jelly as a first-aid application.—*Lancet*, ii/1940, 627.

For first-aid treatment gentian violet jelly with Merthiolate (1 in 5000) is the best application. It is convenient in use and can be applied to the burnt area without any cleansing whatsoever. For hospital treatment, after the burnt area has been thoroughly cleansed, and blistered and dead epidermis removed (under a general anæsthetic), an aqueous solution of Triple Dye is sprayed on the surface; this consists of gentian violet 2%, brilliant green 1%, and neutral acriflavine 1%. This is dried and a second application applied; usually two applications are sufficient.—C. P. G. Wakeley, *Proc. R. Soc. Med.*, 1940, 34, 43.

W. C. Wilson now uses a single application of a 10% solution of silver nitrate, preceded and followed by a 1% solution of gentian violet.—*Proc. R. Soc. Med.*, 1940, 34, 52.

**ENDOCARDITIS.** Details of 7 cases of rheumatic carditis in children treated by intravenous injections. Dose.—25 to 50 ml. of a 0.25% aqueous solution (i.e., 0.005 g. per kilo). Injections given at weekly intervals. Definitely toxic effects occurred in the case of a 5-year old child. Of 10 cases, 8 were definitely improved. With caution as to dose and type of case, the method is safe and worth further trial in the treatment of blood infections.—William Gunn, *Lancet*, i/1927, 127.

**LEG ULCERS.** 15 cases of from 1 to 20 years' duration successfully treated with a 2% aqueous solution, after every other form of treatment had failed. The solution was applied from 3 to 5 times the first day and this procedure repeated for the next two or three days, or until a hard, firm, dry, adherent crust had formed. The solution was permitted to air-dry and the ulcers were not bandaged. As long as the violet-stained crust remained firm, dry, and adherent

it was not disturbed. Portions of crust becoming loose or pocketed were removed, the ulceration cleansed with dry sterile gauze and the solution re-applied as before. Ulcers heal in a comparatively short time and leave scars of a smooth, fine texture. With oedematous ulcers, the oedema must first be brought under control.—F. M. Thurmon and H. Chaimson, *New Engl. J. Med.*, 1935, 216, 11.

**MYCOTIC SKIN AFFECTIONS.** Infectious eczematoid dermatitis, impetigo, folliculitis and furunculosis. A 5% solution in water containing 20% alcohol, applied with a swab.—A. R. McFarland, *Arch. Derm. Syph., N.Y.*, Jan., 1928.

A 2% watery solution is of value in impetigo, impetiginised eczema, intertrigo, eczematoid ringworm of the feet and hands, paronychia (a slightly stronger solution may be used) and seborrhœic dermatitis. In the deep-seated pustular conditions such as furunculosis or syccosis the dye is not of much avail as its action is too superficial.—F. C. Florence, per *Practitioner*, ii/1936, 122.

A highly satisfactory application in intertrigo is 1% gentian violet or malachite green in 25% spirit. This is painted on once a day. Relief is rapid and there is a gradual contraction of the inflamed areas. In some cases the spirit lotion is too drying, and in these cases an ointment containing equal parts of zinc and ammoniated mercury acts well.—R. Gibson, *Med. Pr.*, ii/1936, 566.

A formula consisting of 2% gentian violet and 10% salicylic acid in 95% alcohol is recommended as a local application for ringworm of the scalp due to microsporon of the animal type. The head is first shaved, cleared of all crusts with soap and water and then alcohol, and then painted with the mixture. The lesions are scrubbed clean and painted daily for ten days.—W. F. Spiller *et al.*, *Arch. Derm. Syph., N.Y.*, 1940, 41, 370.

**OXYURIASIS.** Gentian violet, in enteric-coated tablets was found superior to all the other methods of therapy in the treatment of pinworm infestation. The dosage of the drug for adults is two 32 mg. tablets three times a day before meals, and for children 10 mg. a day for each year of apparent age, the total daily amount being divided into three doses. Transient minor reactions, e.g., nausea, vomiting and diarrhoea, occur in some patients and the treatment is contraindicated where there is concomitant infestation with *Ascaris lumbricoides*, cardiac, hepatic or renal disease, alcoholism and diseases of the gastro-intestinal tract.—W. H. Wright and F. J. Brady, *J. Amer. med. Ass.*, i/1940, 861.

**STAPHYLOCOCCAL SEPTICÆMIA.** Startling results may be obtained, but failures are equally numerous. The cases reported total about 40% definitely improved, 20% possibly improved and 40% unimproved. Used in 1 in 200 solution in water, each ml. containing 0.005 g. of dye, a full dose being 45 ml. for a 7-stone patient. More concentrated solutions may cause thrombosis. Initial injection of 0.002 g. per kilo. Sharp temperature reaction, sometimes a chill, following injection. In favourable cases, following fall in temperature, improvement is marked. Value due to its bacteriostatic action in the blood stream.

**THRUSH.** The infection is easily got rid of by a 1% aqueous solution of gentian violet, which should be applied with a soft brush. Even the more serious conditions of thrush can be treated by liberal applications of the gentian violet solution to the mouth and subsequent swallowing of it by the infant.—John Craig, *Practitioner*, ii/1939, 611.

**Methylrosaniline Chloridum (U.S.P. XI Supp. II).** *Syn.* GENTIAN VIOLET, METHYL VIOLET, CRYSTAL VIOLET.

It is described as a mixture of hexa-, penta-, and tetra-methylparosaniline chlorides, soluble about 1 in 35 of water, in alcohol, glycerin and chloroform. Insoluble in ether.

**Crystoflavine (Crookes' Laboratories, London).** Burn lotion containing gentian violet, brilliant green and acriflavine.

**Liquor Tinctorium (B.P.C.).** *Syn.* BONNEY AND BROWNING'S SOLUTION, BLUE PAINT, SOLUTION OF BRILLIANT GREEN AND CRYSTAL VIOLET.

Crystal violet and brilliant green 0.5% w/v of each in equal parts of alcohol and water.

A non-irritant antiseptic for sterilising the skin. Stains may be removed with hypochlorite solution, e.g. eusol.

**Liquor tinctorium** is probably the most powerful skin disinfectant. Bonney's method of preparing the skin of an operation area consists in painting the part, usually six hours before, then applying a compress of lint soaked in the solution and covering with thin waterproof, which is kept in position until the time of operation.—C. H. Browning, *Practitioner*, ii/1940, 296.

**BURNS.** This mixture of dyes should replace tannic acid. Not only is it a perfect antiseptic lotion for deeper burns, but when applied on gauze to burns of the first three degrees it adheres as a firm case quite as occlusive as the tannic acid coagulum. This case separates gradually as the skin heals and leaves an even better scar than tannic acid. Besides sharing with tannic acid the valuable attributes of freedom from re-dressings and from pain it has the following further advantages: it is easier to apply, since it can be put on burns of all degrees, no re-spraying is necessary, and the toilet of the damaged area need not be so thorough; the gauze being bandaged on, the subsequent care of the case is easier; there is little or no risk of effusion beneath the dressing.—A. J. Hobson, *Lancet*, ii/1940, 249.

**Pigment. Cæruleum (N.I.F.).** Crystal violet and brilliant green, of each  $2\frac{1}{2}$  gr., industrial methylated spirit to 1 oz.

**Methylthioninæ Hydrochloridum (B.P., U.S.P. XI).** *Syn.* METHYLTHIONINE CHLORIDE, METHYLENE BLUE, METHYLENUM CÆRULEUM (P. *Helv.* V, Fr. *Cx.*, P. *Jap.* V), TETRAMETHYLTHIONINI CHLORIDUM (P. *Belg.* IV).  $C_{16}H_{18}N_2ClS = 319.8$ .

*U.S.P. XI, P. Helv. V, and Fr. Cx. have  $3H_2O$ .*

**Dose.**—1 to 5 grains (0.06 to 0.3 g.) in pill, cachet or capsule. *U.S.P. XI average dose  $2\frac{1}{2}$  grains.*

It may also be employed intramuscularly or intravenously (*vide infra*), but hypodermically it may give rise to ulcers or abscesses.

Dull dark green crystals, forming an intense blue solution in water.

**Soluble** about 1 in 50 of water; soluble also in alcohol 90% and chloroform.

**Incompatible** with caustic alkalis.

**Distinguish** from the commercial compound with zinc.

**Uses.** Mildly antiseptic and excreted by the kidneys, hence has been used as a genito-urinary antiseptic in cystitis and gonorrhœa. Is also used in these conditions by injection, as 0.1 to 0.2% solution. It has also been given internally in malaria where quinine is not tolerated and in blackwater fever, but it is much inferior to the cinchona alkaloids. It is a feeble analgesic and was formerly advocated for rheumatism, migraine and painful nervous affections. Colonic lavage with the 1 in 5000 to 1 in 1000 solution has been used in dysentery and ulcerative colitis.

In chronic suppurative otitis media and conjunctivitis, 1 in 500 solution is instilled warm. In intertriginous eczemas, 3 to 5% solution. The 5% solution, injected intramuscularly in 1 ml. doses, is used as a test for renal efficiency. It colours urine blue, and faeces become blue on exposure to air. Solutions of methylene blue are largely used as stains for bacteria (*see* Vol. II).

Cyanide poisoning has been successfully treated by injecting intravenously 100 ml. of a 1% solution and the cyanosis due to sulphonamide treatment rapidly responds to methylene blue, either orally or intravenously (*see* p. 937).

**CYANIDE POISONING.** Methylene blue should be tried in every case of cyanide poisoning and should be part of emergency equipment. Amyl nitrite and sodium

tetrathionate may also be used, the former even in conjunction with methylene blue. The balance of evidence is against methylene blue being of any value in CO poisoning.—G. F. Copper, *U.S. Nav. med. Bull.*, 1935, 33, 364.

**Tabellae Methylthioninae Hydrochloridi** (B.P.C.). Contain 2 gr. (0.12 g.).

**Phenothiazine** (the parent substance of the thiazine dyes) has proved to be an effective urinary antiseptic when given orally for a limited period of time in daily doses of 1.5 to 2 g., especially when the pH of the urine is kept acid in a pH range of 4.5 to 5.5 by the administration of ammonium chloride. The maximum total dose should not exceed 15 g. without a rest period, but generally a therapeutic result will be obtained with much less, if benefit is to occur. It is capable of producing secondary anaemia when used continuously in excessive or extra therapeutic doses, and the blood should be examined periodically if medication is continued for long periods. No undesirable effects noted on the gastro-intestinal tract, circulation, kidneys or liver.—Floyd deEds *et al.*, *J. Pharmacol.*, 1939, 63, 371.

**Novaurantia** (B.P.C.). *Syn.* ORANGE G.  $C_{14}H_{12}N_2O_7S_2Na_2 = 452.2$ . Colour Index No. 27.

The disodium salt of benzeneazo- $\beta$ -naphthol-6 : 8-disulphonic acid, occurring as a yellowish-red powder, soluble in water and in alcohol 90%, giving orange coloured solutions.

**Viride Malachitum** (B.P.C.). *Syn.* MALACHITE GREEN.

$2C_{23}H_{25}N_2 \cdot 3H_2C_2O_4$ . Colour Index No. 675.

The oxalate of *pp*-tetramethyldiaminotriphenylcarbinol anhydride, in green crystals with metallic sheen. **Soluble** in water and alcohol 90%. Has antiseptic properties, especially for gram-positive organisms, but brilliant green is now usually preferred.

Stains on the hands with malachite green are easily removed by rubbing with a little cotton wool soaked in alcohol, dilute hydrochloric acid or dilute acetic acid.

**Uses.** Has been employed as an antiseptic dressing, especially in the form of a spray, and particularly in the treatment of war wounds. It should not be applied to mucous membranes. Is more active for gram-positive organisms.

**Cheate's "Green Spray."** *Syn.* SUBLIMATE MALACHITE GREEN SOLUTION.

Equal parts of 2% malachite green in 80% alcohol and 2% mercuric chloride in 80% alcohol. The two solutions are best kept separate and mixed as required.

The spraying must be thorough and the spirit allowed to evaporate before applying the dressing.

[P2-S1] **Pigmentum Viride** (*St. J. H.*).

Malachite green 5 gr., mercuric chloride 5 gr., industrial methylated spirit 6 dr. water to 1 oz.

**Viride Nitens** (B.P.C.). *Syn.* BRILLIANT GREEN.

$C_{27}H_{33}N_2 \cdot SO_4H$ . Colour Index No. 662.

The sulphate of tetraethyldiaminotriphenylcarbinol anhydride, in small golden crystals soluble in water and alcohol 90%.

**Uses.** The dye is an antiseptic and disinfectant and has been much used for the same purposes as acriflavine.

These two dyes had the highest "T.C." (*v.* Acriflavine). Brilliant green differs, however, in that it is not advised to be introduced by injection into closed spaces, and its activity is reduced in the presence of serum. It is also less rapid in action. It differs from crystal violet in being strongly bactericidal to the coli-typhoid group. For wounds a 1 in 1000 to 1 in 2000 solution is used, promoting a vigorous growth of granulation tissue. It may also be used for continuous irrigation of wounds. Septic conditions of the

ears have been treated with brilliant green  $\frac{1}{2}\%$ , mercuric chloride  $\frac{1}{2}\%$  in 90% alcohol, and the 0.1% aqueous solution with 0.25% of allantoin is used as ear drops to promote epithelisation after the radical mastoid operation.

It is a useful epithelial stimulant in various minor injuries and affections, e.g., impetigo, indolent ulcers of various kinds, blisters, etc.

Stains on the skin can be removed with spirit, those on clothes by spirit or washing with soap.

**EPIDERMOPHYTOSIS.** Painting of the affected part daily with 1% brilliant green in rectified spirit of value.—W. Lambert, *Brit. med. J.*, ii/1934, 798.

**SYCOSIS.** Remove crusts with 5% salicylic ointment, followed by epilation of loose pustule-encircled hairs and daily painting with 1% alcoholic solution of brilliant green in 70% alcohol. 53 cases cured after 12 to 25 applications, with no relapses.—*Lancet*, i/1932, 202.

**Brilliant Green Ointment.** Brilliant green 1 or 2% in twice the amount of alcohol 90% and incorporated with soft paraffin. For superficial wounds.

**Brilliant Green Paste (Hey's).** Brilliant green 1, boric acid 275, French chalk 25, liquid paraffin 200. The dye is incorporated in solution in a little spirit. For filling wound cavities.

**Methyl Green, syn. LIGHT GREEN,** is chloromethylhexamethyl-*p*-rosaniline hydrochloride.

**Rubrum Scarlatinum (B.P.C.).** *Syn.* BIEBRICH SCARLET R MEDICINAL, SUDAN IV, *o*-TOLUENEAZO-*o*-TOLUENEAZO- $\beta$ -NAPHTHOL.  $C_7H_7N_2 \cdot C_7H_6N_2 \cdot C_{10}H_8OH$ . Colour Index No. 258. A red dye, with m.p. between  $165^\circ$  and  $185^\circ$ .

**Soluble** in oils and fats, insoluble in water.

**Uses.** To regenerate skin and to hasten epithelisation, has been much employed in the form of an ointment containing 4 to 8% of the substance, though the latter strength is somewhat irritating and should be alternated with a soothing ointment. When used in the treatment of chronic ulcers it is important that the local circulation be good.

There has been some confusion regarding the nomenclature and constitution of the scarlet R dyes, and the above medicinal Biebrich should always be specified.

**INDOLENT ULCERS.** The following dressing applied at least twice daily recommended. Immerse lint for two days in a solution of 20 grains of Biebrich red in a pint of water with 2% powdered allantoin. Allow to dry without wringing or artificial heat and then iron out at low temperature. Cut to size and shape of ulcer.

[P1-51] **Oleum Scarlet et Atropinæ.** Corneal ulcers have been treated by a 5% suspension in castor oil containing 1% atropine.

**Unguentum Rubri Scarlatini (B.P.C.).** *Syn.* UNGUENTUM RUBRUM. 5% in simple ointment. Other strengths (from 2 to 8%) are sometimes used.

**Epithedol (Wyleys Ltd., Coventry).** Ointment of scarlet red 2%, containing also hydroxyquinoline sulphate and chlorbutol. For epithelial regeneration in burns, eczema, etc.

The following scarlet colours have been similarly employed:—

**Oil Scarlet.** *Syn.* CERASINE RED, BENZENEAZOBENZENEAZO- $\beta$ -NAPHTHOL, SUDAN III.

This is also insoluble in water, moderately in alcohol, and very soluble in chloroform and ether and has been found quite satisfactory.

**Non-Staining Scarlet.** *Syn.* *o*-AMINOAZOTOLUENE.

Soluble in oils and fats, insoluble in water. Considered by some to be more efficacious than scarlet red.

"Ordinary" Biebrich scarlet is the sodium salt of *p*-sulphobenzeneazo-*o*-sulphobenzeneazo- $\beta$ -naphthol, soluble in water making an orange-red solution.

**Diacetylaminoozotoluol** (*P. Helv. V, P.G. VI, P. Ned. V Supp. II, P. Spec. X*). *Prop. Name*. PELLIDOL (Bayer Products, London).

$\text{CH}_3 \cdot \text{C}_6\text{H}_4 \cdot \text{N} : \text{N} \cdot \text{C}_6\text{H}_4 \cdot \text{CH}_3 \cdot \text{N}(\text{CO} \cdot \text{CH}_3)_2 = 309.2$ .

Red powder with slight acetous odour. Insoluble in water, soluble in alcohol, ether or chloroform, also in oils, fats, and soft paraffin. A non-staining compound used for the same purposes as scarlet red. Usually applied as a 2% ointment in soft paraffin.

Azodermin, the monacetyl derivative of aminoazotoluol, has also been used for promoting the growth of skin on wounds.

**Trypan Red.** *Syn.* SODIUM 3-SULPHODIPHENYLDISAZOBIS- $\beta$ -NAPHTHYLAMINE-3 : 6-DISULPHONATE. Colour Index No. 438. A brown powder giving a red aqueous solution.

Is active against trypanosomes *in vitro*, but rarely used medicinally.

**Trypan Blue.** *Syn.* SODIUM DITOLYLDISAZOBIS-8-AMINO-*l*-NAPHTHOL-3 : 6-DISULPHONATE.  $\text{C}_{34}\text{H}_{24}\text{O}_4\text{N}_6\text{S}_4\text{Na}_4$ . Colour Index No. 477. A bluish-grey powder giving a violet solution with water. Insoluble in alcohol.

**PARKINSONISM.** Successfully treated by trypan blue 1% intravenously—2 injections of 1 ml. followed by 3 or 4 of 2 ml. with an interval of 3 or 4 days between each two injections and an interval of a month between courses. No ill effects and injections well tolerated.—*Lancet*, i/1932, 1319.

**Tartrazine (B.P.C.).**  $\text{C}_{16}\text{H}_9\text{O}_6\text{N}_4\text{S}_2\text{Na}_2 = 534.2$ .

Colour Index No. 640.

The sodium salt of 4-*p*-sulphobenzeneazo-1-*p*-sulphophenyl-5-hydroxypyrazole-3-carboxylic acid, occurring as an orange-yellow powder. Is used as a colouring for lemonade and lemonade powders, and, in conjunction with orange G, as a yellow colour for foods and medicines.

**Liquor Tartrazinæ Compositus (B.P.C.).** *Syn.* LIQUOR FLAVUS.

Tartrazine 0.75% *w/v* and orange G, 0.25% *w/v*, in glycerin and chloroform water. Used as a yellow colouring agent for mixtures, etc.; 5 m. per oz. is approximately equivalent to 12½ m. of fresh tincture of saffron.

**Auramine.** *Syn.* TETRAMETHYLDIAMINODIPHENYLKETONIMINE HYDROCHLORIDE.  $\text{C}_{17}\text{H}_{21}\text{N}_4\text{Cl} \cdot \text{H}_2\text{O} = 303.7$ .

*Dose.*—½ grain (0.02 g.) has been given *per os*.

A yellow powder soluble in water. The solution is decomposed on boiling or on long standing in the cold, the imino group of the compound being converted into a ketone group by hydrolysis, giving the insoluble Michler's ketone and ammonium chloride.

An antiseptic non-irritant dye for sterilising the skin prior to operation.

**Glauramine (British Drug Houses, London)** is a concentrated solution of auramine in glycerin and alcohol, to be diluted with water immediately before use.

**Sudan Red III.** AMINOAZOBENZENE- $\beta$ -NAPHTHOL.

$\text{C}_{21}\text{H}_{19}\text{N}_3\text{O} = 352.2$ . A brown dye for colouring fats, and in histology.

**Chrysoidine.** DIAMINOAZOBENZENE HYDROCHLORIDE.

$\text{C}_8\text{H}_8\text{N}_2\text{C}_6\text{H}_4(\text{NH}_2)_2\text{HCl} = 248.6$ . An orange dye, slightly soluble.

### Other Common Colouring Matters

**Anchusa (B.P.C.).** *Syn.* ALKANNA, ALKANET ROOT.

The dried root of *Anchusa tinctoria* (Boraginaceæ). Contains 3% red amorphous substance, alkanin. "Red oil" is obtained by macerating alkanna in liquid paraffin 1 in 7.

**Coccus** (B.P., Fr. Cx.). *Syn.* COCHINEAL, COCCUS CACTI.

The dried female insect *Dactylopius coccus* (Hemiptera) containing eggs and larvæ. The insects are reared on various species of *Nopalea* (Cactaceæ). If killed by sulphur or charcoal fumes the insects are silvery in colour ("silver grain") owing to deposit of wax on the surface. If killed by heat the wax is melted and "black grain" cochineal is produced.

**Liquor Cocci** (B.P.C.) contains the colouring matter of 10% w/v of cochineal.

**Tinctura Cocci** (B.P.). *Dose.*—5 to 15 minims (0.3 to 1 ml.). 1 in 10 of alcohol 45%.

**Carminum** (B.P.C., Fr. Cx., P. *Helv.* V).

Red colouring matter containing about 50% of carminic acid,  $C_{17}H_{13}O_{10} = 382.1$ , prepared from cochineal by precipitation with alum.

It is *insoluble* in water, but entirely soluble in aqueous ammonia.

Is used to colour medicinal and toilet preparations and for staining in microscopy.

**Liquor Carmini** (B.P.C.) contains 6% w/v of carmine in a weakly ammoniacal solution. For colouring mouthwashes, etc., 3 or 4 minims per fl. oz. is used.

**Glycerinum Carmini** (B.P.C.) is a similar solution prepared with potassium carbonate.

**Liquor Rosæ Dulcis** (B.P.C.) is a similar preparation of 4% w/v of cochineal containing oil of rose. Is useful for colouring and perfuming preparations.

**Crocus** (B.P.C., Fr. Cx., P. *Jap.* V, P. *Helv.* V). *Syn.* SAFFRON.

The dried stigmas and tops of the styles of *Crocus sativus* (Iridaceæ). Its preparations are used as colouring agents.

Saffron has been employed as an abortifacient for many years and several fatal cases have been recorded. The chief toxic symptoms are flushing of the face, epistaxis, vertigo, vomiting, bradycardia and stupor. Death (after profuse metrorrhagia and abortion) following use of 24 gr.—P. Fasal and G. Wachner, *Wien. klin. Wschr.*, 1933, 747.

**Glycerinum Croci** (B.P.C.). 1 in 40 in glycerin and alcohol 60%.

**Syrupus Croci** (B.P.C.). Glycerin of saffron 1, syrup 7. About 1 in 8 is sufficient for colouring mixtures.

**Tinctura Croci**. 1 in 5 of alcohol 60%.

## BALSAMUM PERUVIANUM

B.P., U.S.P. XI, Fr. Cx., P. *Jap.* V, P. *Helv.* V, P. *Dan.*

*Dose.*—5 to 15 minims (0.3 to 1 ml.).

A balsam exuded from the trunk of *Myroxylon Pereira* (U.S.P. XI, *Toluifera Pereira*), after beating and scorching. Occurs as a viscid liquid containing cinnamain and cinnamic acid.

*Soluble* in chloroform, partially soluble in ether, light petroleum and glacial acetic acid; soluble 1 in 1 of alcohol 90%, but solution becomes turbid on adding 2 of alcohol 90%. Insoluble in water.

*Uses.* Inhalation of the vapour from a few drops of a solution of balsam of Peru 1 in alcohol 2, in a little hot water, is useful in



pharyngitis. As a dressing to wounds, if aseptic, may be left for 20 days if necessary. Scabies has been treated with a paint of balsam 3, glycerin 1. But test for albumin in urine both before and during treatment.

[P.] **Lotio Balsami Peruviani.** In alopecia a preparation of Peru balsam 1 dr., spirit of rosemary 1 oz., tincture of cantharides 4 dr., pilocarpine nitrate 2 gr., almond oil 1 oz. has been employed. This is applied at night and washed off next morning with a borax and spirit lotion.

**Unguentum Peruvianum (B.P.C.).** 12½% in simple ointment.

**Unguentum Balsami Peruviani.** Balsam of Peru 20, trikresol 5, soft paraffin *q.s.* to 100. Mix warm.

For scabies an ointment containing Peruvian balsam and sublimed sulphur 4½% of each, in soft paraffin.

**Ammoniacum (B.P.C., Fr. Cx.).**

*Dose.*—5 to 15 grains (0.3 to 1 g.).

Gum-resin from *Dorema Ammoniacum* (Umbelliferæ). In pale yellow tears or nodular masses with characteristic odour and acrid taste. Is used in chronic bronchitis with viscid secretion to facilitate expectoration.

**Mistura Ammoniaci (B.P.C.).**

*Dose.*—½ to 1 ounce (15 to 30 ml.).

Contains the equivalent of 13 gr. of ammoniacum per oz.

**Balsamum Tolutanum (B.P., U.S.P. XI, Fr. Cx., P. Jap. V, P. Helv. V, P. Dan.).**

*Dose.*—5 to 15 grains (0.3 to 1 g.).

Obtained from the trunk of the *Myroxylon Toluifera* (U.S.P. XI, *Toluifera Balsamum*) (Leguminosæ). Recently prepared is soft, but becomes brittle in cold weather. It contains benzoic and cinnamic acids both free and esterified with benzyl alcohol.

**Soluble** 1 in 1 of alcohol 90%, and in acetone, ether, chloroform and solutions of fixed alkalis, usually leaving some residue.

Is antiseptic and expectorant.

**Liquor Tolutanus (B.P.C.).** 1 part mixed with 7 parts of syrup gives a preparation similar to syrup of tolu (B.P.).

**Syrupus Tolutanus (B.P., Fr. Cx.).** *Dose.*—½ to 1 drachm (2 to 4 ml.).

Made by digesting the balsam and water on the water-bath during ½ hour and dissolving sucrose in the filtered liquid.

**Syrupus Balsami Tolutani (U.S.P. XI).** *Syn.* SYRUPUS TOLU (U.S.P. X). *Average dose.*—2½ drachms (10 ml.). Tincture of tolu balsam 5, sucrose 82, water to 100.

**Tinctura Tolutana (B.P.).**

*Dose.*—½ to 1 drachm (2 to 4 ml.). 1 in 10. In mixtures the resin must be suspended with mucilage.

**Tinctura Balsami Tolutani (U.S.P. XI).**

*Average dose.*—30 minims (2 ml.).

Balsam of tolu in alcohol, 1 in 5. *Fr. Cx.* is similar, but made with 80% alcohol.

**Balsamum Gurgune.**—Gurjun Balsam, Wood Oil. *Dose.*—½ to 2 drachms. Obtained from *Dipterocarpus turbinatus* and other species. Contains from 40 to 80% of volatile oil, and is used in gonorrhœa and as an expectorant given with malt extract.

**Styrax** (B.P., U.S.P. XI, P. Helv. V). Syn. STYRAX PRÆPARATUS, BALSAMUM STYRAX LIQUIDUS (P. Dan., P. Jap. V), STYRAX DEPURATUM (Fr. Cx.).

*Dose.*—10 to 30 grains (0·6 to 2 g.).

The balsam obtained from the wounded trunk of *Liquidamber orientalis*, purified by dissolving in alcohol, filtering and evaporating. U.S.P. XI allows it to be obtained also from *L. styraciflua*. A thick brown liquid containing not less than 30% of balsamic acids. Contains cinnamyl cinnamate (styracin) and other cinnamic acid compounds together with a large proportion of storesin,  $C_{30}H_{55}(OH)_2 = 538\cdot5$ .

**Soluble** in alcohol 90%, ether, carbon disulphide, chloroform and glacial acetic acid.

Is used as an ointment containing 20 to 25% in scabies and parasitic skin diseases.

**Pommade au Styrax** (Fr. Cx.). Melt colophony 29, yellow beeswax 16, and elemi resin 16. Add styrax 16, and olive oil 29.

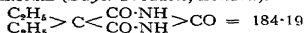
[P2] **Storaxol** (Parke, Davis, London). Storax, resorcinol, menthol, camphor, phenol (22 gr. per oz.), and precipitated sulphur in a wool fat and soft paraffin base. For use in acne, sycosis, etc.

## BARBITONUM

B.P., P.G. VI, Fr. Cx., P. Helv. V, P. Jap. V, P. Ned. V, P. Svec. X, P. Dan., U.S.P. XI, P. Belg. IV, F.E. VIII, P. Ital. V.

Syn. and Prop. Name. 5 : 5'-DIETHYLBARBITURIC ACID, DIETHYLMALONYLUREA, MALONUREA, BARBITALUM, MALONAL.

VERONAL (Bayer Products, London).



[P1] "Barbituric acid; its salts; derivatives of barbituric acid; their salts; compounds of barbituric acid, its salts, its derivatives, their salts, with any other substance."

[S1] "Barbituric acid; its salts; derivatives of barbituric acid; their salts; compounds of barbituric acid, its salts, its derivatives, their salts, with any other substance."

[S4] "Barbituric acid; its salts; derivatives of barbituric acid; their salts; compounds of barbituric acid, its salts, its derivatives, their salts, with any other substance."

*Dose.*—5 to 10 grains (0·3 to 0·6 g.)—should be taken with a hot drink.

P.G. VI max. single dose 0·75 g., max. per diem 1·5 g.; Fr. Cx., P. Belg. IV, P. Jap. V and F.E. VIII, 0·5 and 1 g. respectively; P. Ital. V, 1 and 2 g. respectively.

NOTE.—The name "Barbitone" in Fr. Cx. is applied in error to phenobarbitone.

Caution.—5 grains is sufficient for an ordinary case of insomnia, 50 gr. might be regarded as the average minimum fatal dose, although as little as 10 gr. has proved fatal (*vide infra*).

**Manufactured** by condensing urea with ethyl diethylmalonate.

A white crystalline powder melting at 189° to 192° (U.S.P. XI 187° to 190°).

**Soluble** 1 in about 170 of water, 1 in 12 of boiling water, 1 in 8½ of alcohol 90%, 1 in 25 of ether, 1 in 35 of chloroform. Boiling with alkalis decomposes it. Also soluble in acetone and ethyl acetate.

**Toxic Effects.** Barbitone is excreted slowly, and bowels and kidneys should be functioning adequately. It is cumulative, and regular administration may cause chronic poisoning characterised by headache, visual disturbance and weakness, with anæmia and albuminuria. Acute poisoning is characterised by a brief period of headache, ataxia and muscular twitching, followed by sleep rapidly passing to coma. Later the breathing becomes slow and shallow, there is œdema at the bases of the lungs, and bronchopneumonia may set in. Nystagmus is frequently present, and there is complete suppression of urine. In a few individuals idiosyncrasy exists, and quite small doses produce skin eruptions of various kinds.

Barbitone taken every night is liable to produce mental and moral changes with suicidal tendencies, also diplopia with visual paralysis and the kind of speech found in G.P.I.: hæmatoporphyrinuria is a characteristic of phenobarbitone poisoning. Continued administration of these drugs produces pathological changes in the central nervous system, which, although they usually disappear when the drug is discontinued, may become permanent.

A man of 120 pounds (54 kg.) bodyweight survived a total dose of 18 g. (270 gr.) of sodium barbital, taken with suicidal intent. The poisoning was characterised by a deep coma of six days' duration, a very high temperature and rapid pulse and respiration, in contrast to the usual picture of severe depression of temperature and respiration.—D. K. Chang and M. L. Tainter, *J. Amer. med. Ass.*, i/1936, 1386.

The alleged dangers of the barbiturates. Statistical tables giving details of all fatalities associated with barbituric drugs recorded up to the end of 1932. Of the total of 5147 recorded suicides in 1931 only 13, or 0.26%, were attributed to barbiturates. Up to the end of 1932 there is no case on record in which barbiturates, either a single dose or repeated doses of therapeutic magnitude, have caused death in the absence of complicating factors.—R. D. Gillespie, *Lancet*, i/1934, 337.

"The Battle of the Barbiturates." A protracted and voluminous correspondence.—See *Lancet*, i/1934.

Toxicology of barbiturates.—H. T. Roper-Hall, *Proc. R. Soc. Med.*, Jan., 1936.

The margin of safety between the hypnotic dose and the lethal dose as represented by the ratio M.L.D./M.Th.D. is: Luminal 1.3; Barbitone 1.6; Soneryl, Nembutal and Phanodorm 2.4; Dial 2.5; Evipan 5. It would not appear very safe to employ Luminal in full hypnotic doses.—N. Mutch, *Brit. med. J.*, i/1934, 321.

**Antidotes to Barbiturate Poisoning.** Empty stomach by stomach tube, using 2 gallons of warm water, since emetics are probably of little use. Keep patient warm and try to keep him awake, but he must not be walked about. Give hot, strong coffee. Strychnine, ½ gr., nikethamide, 5 to 15 ml. of 25% solution, and alcohol, should be injected and repeated as required; alternatively,

microtoxin in doses of from 1 to 10 mg. intramuscularly or intravenously in 0.2% aqueous solution (for further details see page 934). Fluids must be given freely; if coma is prolonged, patient must be fed by stomach tube with coffee, dextrose, peptonised milk, etc. Dextrose in saline may be given by rectum, and saline intravenously. Artificial respiration should be started early and kept up for a long time. Oxygen with 7% carbon dioxide inhalations may be necessary. Lumbar and cisternal puncture and drainage to remove the poison may be carried out every 12 or 24 hours, especially if "veronal pneumonia" has set in.

Veronal is excreted slowly and unchanged in the urine: in cases of poisoning increase the efficiency of the kidneys by injection of large volumes of 5% to 10% dextrose solution. A woman who had taken 60 grains was given  $1\frac{1}{2}$  litres 5% dextrose 4 hours later. In 6 hours she passed 1100 ml. urine, and 11 hours later showed no symptoms of the drug.—*Amer. J. Pharm.*, 1930, 599.

A fatal case in which 0.62 g. of strychnine were given without any signs of intoxication by it.—L. Raymond and J. Delay, per *Lancet*, i/1934, 93.

Alcohol injections intravenously of value. A patient in a state of slight coma from having taken 1.5 g. of Gardenal was given 20 ml. of 30% alcohol intravenously once an hour, and awoke to complete consciousness on the fourth injection. Animal results confirmatory of clinical observations. Probably at least 30 ml. of 30% alcohol should be given hourly till patient wakes.—Prof. Carrière, C. Hunez and P. Willoquet, *Bull. Acad. Méd.*, No. 18, 1934, per *Lancet*, i/1934, 1243.

Treatment by large doses of strychnine,  $\frac{1}{4}$  to  $\frac{1}{2}$  gr., repeated hourly if necessary, with Coramine injections or carbogen (oxygen and carbon dioxide) inhalations as respiratory stimulants.—C. Flandin, F. Joly and J. Bernard, per *Brit. med. J.*, ii/1934, 263.

Treatment of acute barbiturate poisoning by washing out stomach with animal charcoal and sugar-lime; Coramine injected; camphor for convulsions; large doses of strychnine intravenously; oxygen inhalations; infusions with adrenaline and insulin.—Hans Fischer, *Schweiz. med. Wschr.*, 1935, 65, 441.

The third day in a severe case of Veronal poisoning is usually the turning point, the fate of the patient depending on the behaviour of the kidneys. During the first two days there is as a rule some excretion of urine, and it is only on the third day that anuria is apt to set in. This anuria is evidently connected with the inadequate intake of fluids, which may be repaired by giving from 2 to 4 litres a day of Ringer's solution subcutaneously, which usually results in a profuse excretion of urine within twelve hours and the tiding of the patient over the critical anuria.—G. Sack, *Dtsch. med. Wschr.*, ii/1936, 2082.

The intravenous injection of 4% sodium bicarbonate solution hastens excretion.—C. Henze, *Dtsch. med. Wschr.*, i/1936, 1878.

**Contraindications**, or indications for special caution, are old age, genito-urinary disease, liver disease, advanced disease of heart or lungs, severe toxæmia, and idiosyncrasy.

Owing to the risk of pneumonia in individuals receiving large doses of barbiturates, they should be withheld in the presence of inflammation of the lungs, operations for empyema and in catarrhal conditions of the bronchial and upper air passages. Also when efficiency of the liver or kidneys is affected by toxic blood conditions, by local inflammation of these organs, or by other diseases such as eclampsia or cirrhosis.—H. W. Featherstone, *Brit. med. J.*, i/1934, 326.

**Uses.** Sedative and hypnotic in nervous restlessness, insomnia and depression, for maniacs and in cardiac trouble. In therapeutic doses it does not affect temperature or respiration. Produces sleep without subsequent depression. Tolerance to it may be established in some cases, and prolonged use may lead to addiction and chronic poisoning. For insomnia it should be taken 2 hours before retiring.

Barbiturates do not relieve pain, and in insomnia due to this cause they are given in combination with an analgesic such as amidopyrine.

The barbiturates are effective against poisoning by strychnine and picrotoxin.

If a phenyl group,  $C_6H_5$ , is used to replace one of the ethyl groups in barbitone, the drug seems to acquire special depressant power over the motor cortex (e.g., Luminal in epilepsy).

If sodium is added to the barbituric nucleus without disturbing the essential ring formation the product becomes soluble, giving greater speed in action and allowing of its injection (e.g., Sodium Soneryl, Sodium Amytal, Sodium Evipan).

The introduction of bromine into the barbituric nucleus (as in Pernocton) acts as a preventive to the state of excitement sometimes preceding narcosis. —N. Mutch, *Brit. med. J.*, i/1934, 321.

[P1-S1-84] **Tabellæ Barbitoni (B.P.C.)**. Contain 5 grains (0.3 g.).

[P1-S1-84] **Tabellæ Barbitoni et Amidopyrinæ (B.P.C.)**.

**Dose.**—1 tablet. Contains 2 gr. of barbitone and 4 gr. of amidopyrine.

[P1-S1-84] **Veramon (Schering, London)**. A combination in tablet form of amidopyrine and a molecular compound of amidopyrine with barbitone. Analgesic in neuralgias, migraine, dysmenorrhœa, biliary colic, and all forms of pain. **Dose.**—Adults, 1-2 tablets; children,  $\frac{1}{2}$ - $\frac{3}{4}$  tablet. The effect sets in after about 20 minutes and lasts for 4-5 hours.

[P1-S1-84] **Veropyron (Richter, London)**. Tablets containing barbitone  $1\frac{1}{2}$  gr., amidopyrine  $3\frac{1}{2}$  gr., and tablets containing barbitone  $2\frac{1}{2}$  gr., amidopyrine  $5\frac{1}{2}$  gr. **Dose.**—1 or 2 tablets.

[P1-S1-84] **Barbitonum Solubile (B.P.)**. *Syn. and Prop. Names.* BARBITALUM SOLUBILE (U.S.P. XI, P. *Helv.* V, P. *Ned.* V, P. *Jap.* V), MEDINAL (Schering, London) (P.G. VI, P. *Svec.* X, P. *Ital.* V), VERONAL-SODIUM (Bayer Products, London). Graphically it may be represented thus:—



**Dose.**—5 to 10 grains (0.3 to 0.6 g.) dissolved in water either before or not less than 1 hour after meals. In most cases 5 grains is sufficient for an adult. P.G. VI has max. single dose 12 grains approx. (i.e., the same as for barbitone).

Hypnotic effect is also obtained by the use of suppositories medicated with 0.4 to 0.5 g.

Even small doses, e.g., 1 grain 3 times a day, in some instances, produce a lengthy sleep—at night.

It is stated that toxic signs do not appear with less than 15 grains daily, whilst an adequate sedative effect at the menopause is obtained with 1 to 2 grains 3 times a day, half an hour after meals.

White crystals *soluble* 1 in 6 of cold water; slightly soluble in alcohol 90%, insoluble in ether or chloroform. It has properties and uses similar to barbitone *antea*. It is useful in sea-sickness.

**Incompatible** with ammonium salts, e.g., the bromide, and with acids, also with chloral hydrate. In preference, give it alone.

Solutions of soluble barbitone decompose on heating, forming crystals of diethylacetyl urea,  $(C_2H_5)_2CH \cdot CO \cdot NH_2 \cdot CO \cdot NH_2$ . If the compound is prepared with more than the minimum quantity of alkali, solutions decompose below  $100^\circ$ , otherwise they will withstand short heating at  $100^\circ$  and can be sterilised by tyndallisation but not by autoclaving.—A. E. Bailey, *Pharm. J.*, i/1936, 620.

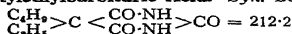
[P1-81-84] **Tabellæ Barbitoni Solubilis (B.P.C.)** contain 5 gr. (0.3 g.).

[P1-81-84] **Neurinase** (*Genevrier, Neuilly; Wilcox, Jozeau, London*). Preparation of soluble barbitone and extract of valerian. 1 dr. contains about 2 gr. of soluble barbitone and  $\frac{1}{2}$  gr. of extract of valerian. *Dose*.—1 drachm in the morning and 1 to 4 drachms at bedtime. For nervous insomnia and neurasthenia. Also available in tablets, each containing 3.3 gr. of soluble barbitone.

[P1-81-84] **Valitone Elixir** (*Roberts & Co., London*). Elixir containing soluble barbitone  $2\frac{1}{2}$  gr. and inodorous fluid extract of valerian 3m. per dr. In insomnia, delirium and as a pre-operative hypnotic. *Dose*.—1 to 4 drachms in a cupful of hot water.

[P1-81-84] **Veronigen** (*Hewlett, London*). *Dose*.—1 drachm (4 ml.) diluted, about 1 hour before going to bed. For nervous sleeplessness in children 10 to 20 minims diluted. A liquid preparation of barbitone as hypnotic.

[P1-81-84] **Butylethylbarbituric Acid**. *Syn.* BUTOBARBITAL.



*Dose*.—1 to 2 grains (0.06 to 0.12 g.) produces sleep in half an hour. It may be given at any time, but in no case less than  $\frac{1}{2}$  hour after food. A larger dose, *e.g.*, 3 grains (0.2 g.) gives a deep sleep lasting some time. In pain from wounds 3 to 4 grains may be used. In delirium 2 grains. Max. in 24 hours, 6 grains.

A white, crystalline powder with slight bitter taste. Readily **soluble** in alcohol; soluble 1 in 300 of water. Sedative and hypnotic for use in insomnia and in nervous conditions. May also be used as a basal hypnotic. Said to be three times as active as barbitone.

[P1-81-84] **Etoval** (*Richter, London*). Butylethylmalonurea. Tablets contain  $1\frac{1}{2}$  gr. *Dose*.—1 or 2 tablets. Sedative and hypnotic.

[P1-81-84] **Soneryl Tablets** (*Pharmaceutical Specialities (May & Baker) Ltd., London*) contain  $1\frac{1}{2}$  gr. of butylethylbarbituric acid.

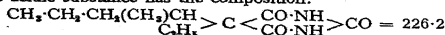
[P1-81-84] **Soneryl Sodium** is the sodium derivative of Soneryl, and is available in capsules containing 0.15 g. ( $2\frac{1}{2}$  gr. approx.). For basal narcosis and in obstetrics.

A reliable basal hypnotic producing sleep or drowsiness in 95% of cases when administered by mouth one hour before the induction of general anaesthesia. Optimum dose varies from 0.6 to 0.9 g. *per os*. Depression of respiration in a few instances and restlessness in 10% of cases. Has not been given in senility, pulmonary disease, renal impairment or arteriosclerosis.—S. E. Birdsall, *Brit. med. J.*, i/1933, 871.

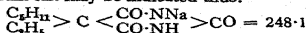
[P1-81-84] **Sonalgin** (*Pharmaceutical Specialities (May & Baker) Ltd., London*). Tablets containing Soneryl  $1\frac{1}{2}$  gr. and phenacetin  $3\frac{1}{2}$  gr.

[P1-81-84] **Pentobarbitalum Solubile (U.S.P. XI Supp. II)**. *Syn. and Prop. Name.* PENTOBARBITAL SODIUM, SODIUM iso-AMYTAL, SODIUM ETHYLMETHYLBUTYLBARBITURATE, NEMBUTAL (*Abbott Laboratories, London*).

The acidic substance has the composition:



The sodium salt may be indicated thus:



A white, crystalline powder, with slightly bitter taste. Very *soluble* in water, freely in alcohol, practically insoluble in ether. Aqueous solutions are alkaline to litmus.

*Dose*.—As a hypnotic  $1\frac{1}{2}$  gr. *per os* or *per rectum* is sufficient. As a pre-anæsthetic and basal hypnotic give one capsule ( $1\frac{1}{2}$  gr.) the evening before and one or two 30 minutes before operation. In obstetrics, the usual dose is 4 or 5 capsules (6 to  $7\frac{1}{2}$  gr.) in primipara, and 3 in multipara, given after there is definite dilatation of the cervix with definite and regular uterine contractions at not more than 5-minute intervals. For intravenous or intramuscular use to control convulsions in strychnine poisoning and tetanus, or in emergency operations, not more than  $7\frac{1}{2}$  grains are dissolved at the time of use in 10 ml. of water, and injected at the rate of 1 ml. per minute.

Intravenous injections must be freshly made; aqueous solutions decompose on standing. On boiling, precipitation occurs.

When given as a pre-anæsthetic in young children, suppositories have been found better than oral or intravenous administration, the dosage, excluding children of 1 year, being 1 grain per year up to a total of 6 grains for children of 6-8. After 8 the drug may be given orally. The suppositories take from 2 to 4 hours to act. Used successfully in 200 cases with no unpleasant after-effects.—R. Jarman, *Brit. med. J.*, i/1936, 236.

ANTIDOTES TO SUBLETHAL AND LETHAL DOSES OF PENTOBARBITAL, CHLORAL HYDRATE AND AVERTIN. The order of practical usefulness of the several therapeutic measures, judged by the degree of improvement in respiration, circulation and reflex excitability, degree of shortening of the usual stages of recovery and the margin of safety of effective dosages of each agent, from high to low, is as follows: picrotoxin, Metrazol, ephedrine, artificial respiration, Coramine, Icoral, strychnine and caffeine sodio-benzoate. The most satisfactory therapeutic measures included combined medication with ephedrine and either picrotoxin, Metrazol or Coramine. Tolerance to these preparations parallels the degree of depression present, particularly with the convulsants. The dosage and frequency of administration of the antagonists must be gauged by the duration of the optimal response observed and the relative need for supportive treatment. Artificial respiration, especially with gas mixtures containing 5 to 10% of carbon dioxide, is highly effective as a single resuscitation measure against lethal doses of these hypnotics.—O. W. Barlow, *J. Pharmacol.*, 1935, 55, 1.

Nembutal is a renal poison. The kidneys stop excreting, with consequent suppression of urine. Four cases of fatal suppression of urine from doses of Nembutal of less than 10 grains. The only thing that will save a person with pneumonia due to barbituric acid drugs is lumbar puncture and the draining off of a good deal of cerebrospinal fluid.—Sir W. Willcox, *Brit. med. J.*, i/1933, 144.

It would appear to be extremely unwise to administer morphine or Omnopon in conjunction with basal narcotics. Two deaths: one with Avertin plus  $\frac{1}{2}$  gr. of morphine and  $1\frac{1}{8}$  gr. of hyoscine, hypodermically, and one with Nembutal (orally) with morphine  $\frac{1}{2}$  gr. and atropine  $1\frac{1}{16}$  gr.—J. M. McNeill Love, *Brit. med. J.*, i/1934, 327.

Danger almost non-existent if not more than  $\frac{1}{2}$  gr. of morphine is given.—G. Keynes and C. L. Hewer, *ibid.*, 400.

*Uses*. Soluble pentobarbital is similar in action to barbitone, but is effective in smaller doses. It is mainly used as a basal narcotic in conjunction with inhalation anæsthesia, being the barbiturate of choice for this purpose owing to its brief duration of action and its high margin of safety. It has also been widely used in conjunction with chloral hydrate or hyoscine hydrobromide for alleviating the pains of childbirth.

Order of hypnotic efficiency (in conjunction with nitrous oxide)—Nembutal, Avertin, Phnodoform, Pernocton. Avertin safest, but efficiency decreased owing to short duration of narcosis.—O. W. Barlow and co-workers, *J. Pharmacol.*, Apr., 1931, 377.

Placed in the following order of merit as basal hypnotics—Nembutal, Sodium Amytal and Pernocton. Nembutal the most outstanding anæsthetic drug to date.—I. W. Magill, *Lancet*, i/1931, 353.

As basal pre-anæsthetic hypnotic Nembutal intravenously in 108 cases—better than Amytal or Pernocton. Effect can be increased by giving morphine simultaneously.—S. Rowbotham, *Lancet*, i/1931, 439.

Oral Nembutal is a great boon as a basal anæsthetic in children. The dose should be small (1 grain or less for a child of 4), given when possible at night, so that the child falls asleep in bed and general anæsthesia can be induced without waking him. The powder may be dissolved in a teaspoonful of syrup or cane sugar in warm water, to mask the bitter taste. If the barbiturate is not effective, or is vomited, a very small dose of Avertin (e.g., 0.05 g. per kilo) may be given. Of value for such procedures as the setting of fractures, repeated lavage of nasal sinuses, and multiple operations for cellulitis or pyæmia.—H. W. Featherstone, *Brit. med. J.*, i/1934, 324.

CHILD BIRTH. Combined oral use of Nembutal and chloral hydrate gave 62% of painless labours in 60 cases without ill-effects to mother or children. Initial dose (when os uteri is two-fifths dilated and regular pains present) Nembutal 3 gr., chloral hydrate 30 gr. (in 3 oz. of sweetened home-made lemonade). First "repeat" dose of 1½ gr. and 30 gr. respectively after 2 hours, and subsequent similar doses at 3-hourly intervals, to a total of 7½ and 120 gr., in 12 hours. Chloral given 10 minutes after Nembutal to obviate vomiting. Not contraindicated in heart disease or albuminuria. May be given by midwives.—J. V. O'Sullivan and W. W. Craner, *Lancet*, i/1932, 119.

Nembutal and chloral the most reliable means for obtaining complete amnesia in labour for the practitioner who cannot spend many hours with his patient.—A. M. Claye and D. W. Currie, *Lancet*, i/1932, 1175.

From an analysis of 100 cases it is concluded that Nembutal, given in combination with chloral, is of undoubted value, especially in placid women with strong distressing pains. Best given between 3 and 5 hours before delivery. Of very doubtful value in nervous or hysterical patients. Nembutal 3 gr. in capsules by the mouth, followed by chloral hydrate 22 gr. as a syrup, perfectly safe. Repeat dose, Nembutal 1½ gr. and chloral hydrate 22 gr., in 3 hours.—F. C. Kelly, *Lancet*, ii/1933, 693.

Combined use of pentobarbital sodium and scopolamine hydrobromide to allay the pain of labour in 1415 cases. When the patient is in labour, regardless of the amount of dilatation of the cervix, she is given 7½ gr. of pentobarbital sodium in 5 separate capsules with a pin hole in each (it is not so effective when given in one capsule as it may form an insoluble mass). Five minutes later give 2 g. of sodium bicarbonate in water to alkalise the stomach. When the pentobarbital sodium is given, scopolamine hydrobromide ½ gr. is administered hypodermically. Patients smaller than the average have only 6 gr. of pentobarbital sodium initially, but the initial dose should be large and the patient must pass quickly through the excitement stage, and the condition maintained by an additional 1½ gr. every two or three hours. This additional amount is necessary because the drug is constantly oxidised in the body. The initial dose for large women is 9 gr. Constant supervision is necessary, and the nurse must not leave the bedside until about five hours after delivery. In the case of extreme restlessness between pains a little more pentobarbital sodium may be administered, but never more than 3 gr. additional; if she is still restless no other drugs are administered. When the patient is ready for delivery she is given ethylene. If the patient is restless after coming out of the gas she may be given ½ gr. of morphine hypodermically. The treatment is contraindicated if the patient is in rapid labour, and in the presence of a full stomach, infection of the respiratory tract, prematurity or heart disease. Maternal mortality and morbidity are not increased, and infant mortality is not increased. It is a hospital procedure only, and should not be used in the home.—C. E. Galloway *et al.*, *J. Amer. med. Ass.*, ii/1936, 1707.

The following combination of drugs administered according to the technique outlined is efficient and safe. The patient is sent to the hospital as early in labour as possible, and enemas are given to cleanse the bowels. She is told she can have medication as soon as she begins to feel uncomfortable as the result of



contractions. The initial dose of Nembutal in capsules will be  $4\frac{1}{2}$  to 6 gr., depending on the weight of the patient, and will be accompanied by  $\frac{1}{16}$  gr. of scopolamine hypodermically. The patient is then placed in a quiet darkened room with a competent attendant who will remain with her until she is roused following delivery, and will remain in constant touch with the physician. One hour following the initial medication another dose of Nembutal may be given, depending on the patient's condition. A maximum of 3 gr. is usually all that is necessary; this will be given by rectum, the capsules being punctured by a needle to facilitate absorption. Another dose of scopolamine will be given at this time,  $\frac{1}{16}$  gr. (if a marked flushing or a distinct rise in the pulse rate followed the initial dose this will be omitted). From then on Nembutal is given in  $1\frac{1}{2}$  gr. doses when indicated. The total dose during labour should probably not exceed  $10\frac{1}{2}$  gr. If marked restlessness occurs it is advisable to use paraldehyde or ether by rectum, 8 to 16 ml. of the former or 60 ml. of the latter. When the patient is ready for delivery a nitrous oxide and oxygen mixture is used with the addition of what ether is necessary.—B. F. Cornwall, *New Engl. J. Med.*, ii/1939, 853.

**MENTAL CONDITIONS.—NEMBUTAL SUPPOSITORIES.** Of value in all types commonly seen in a mental hospital. Individual response tested by preliminary dose of 2 gr. at bedtime—usually resulting in 6 hours sleep. In certain mania states the dose needs to be increased to 6 grains, which is safe and usually effective. Most valuable in the treatment of acute anxiety states and good results in agitated melancholia and senile confusion.—J. S. Horsley, *Brit. med. J.*, 1936, 283.

**TETANUS.** Several cases of tetanus have been controlled by intravenous Nembutal: at least two with a successful cure.—H. W. Featherstone, *Brit. med. J.*, i/1934, 325.

[P1-81-84] **Pentothal** (*Abbott Laboratories, London*). *Syn.* PENTOTHAL ACID. (Supplied in 4 gr. tablets.)

*Dose.*—4 to 8 grains (0.25 to 0.5 g.).

Pentothal is ethyl-(1-methylbutyl)-thiobarbituric acid.

**Uses.** Small doses are sedative, medium doses hypnotic, and large doses anaesthetic. It is employed as a basal anaesthetic, and has been found suitable for producing surgical anaesthesia of short duration, and for inducing analgesia and amnesia during childbirth. Respiration is lessened by full anaesthetic doses, but is almost unaffected by the doses recommended for basal anaesthesia. Its chief practical advantage is its certainty of action when given by the mouth.

The main chemical difference between the acid and the salt (Pentothal Sodium) is in the much greater solubility of the latter, so that the acid is relatively stable. The dosage, however, needs careful arrangement and the best results are achieved by giving 8 gr. three hours before operation, repeating the dose at intervals of an hour, either once or twice according to the effect. Doses of 8 gr. given three and two hours before operation give better results than a single dose of 16 gr. The drug is rapidly eliminated.—*Lancet*, ii/1938, 1072.

**CHILDBIRTH.** Pentothal acid has been given to a series of 200 women with very good results. The patient sleeps between pains and there is a reasonable degree of analgesia and some amnesia. No harm comes to mother or child and labour is not prolonged. The patient is given 6 to 8 gr. of pentothal acid when the pain begins to cause genuine discomfort. This is repeated 45 minutes later, and from then a dose of 2 to 4 gr. is repeated every half to one hour up to as near delivery as is convenient. By the time delivery takes place the patient has usually had 25 to 35 gr. and is in a drowsy, placid state.—G. C. Steel, *Lancet*, ii/1939, 251.

[P1-81-84] **Pentothal Sodium** (*Abbott Laboratories, London*).  $C_{11}H_{17}N_2O_2SNa = 264.3$ . (Supplied in 0.5 or 1 g. ampoules with ampoules of water.)

*Dose.*— $1\frac{1}{2}$  to  $2\frac{1}{2}$  grains (0.1 to 0.15 g.) as a 5% solution for intravenous injection.

The sodium salt of ethyl-(1-methylbutyl)-thiobarbituric acid, occurring as a yellow, crystalline powder, with a sulphur-like odour.

**Soluble** in water giving an alkaline gaseous solution (it is important to see there is no precipitate); also soluble in alcohol, but insoluble in benzene and ether.

**Contraindications.** It is not employed where there is any marked interference with the respiratory function; it is rarely employed for patients under 15 and seldom for patients below 10 years of age; it is contraindicated in the presence of cardiac dysfunction to the point of dyspnoea and where there is varicosity central to the point of injection; manipulations disturbing pharyngeal and laryngeal reflexes preclude its advisability; it should be employed with caution where there is definite deviation from normal in the oxygen-carrying capacity of the blood (*e.g.*, in severe anaemia) and its use is inadvisable in the presence of gross hepatic damage.

**Uses.** The action and uses of Pentothal sodium are similar to those of soluble pentobarbital, except that Pentothal sodium is effective in smaller doses and the action is of briefer duration. It is employed intravenously as a rapidly acting general anaesthetic for use in short operations. It is not recommended for use in major operations.

It is used as an intravenous anaesthetic, 3 ml. usually being sufficient for minor operations. It may be given either as a single dose (for an operation likely to last 10 to 20 minutes), in repeated doses (a second or even third dose may be given), or by continuous intravenous infusion. The induction period is as dramatic, smooth and pleasant as with Evipan, without the twitching or jactitation seen with the latter, and with less fall in blood pressure. The main disadvantage is that it is more depressant to the respiratory centre. The recumbent position is the safest for administration. Pre-medication with barbiturates not advisable. Coramine the most reliable antidote in case of collapse. Used in over 1000 cases.—R. Jarman and A. L. Abel, *Lancet*, i/1936, 422.

Analysis of 100 cases. Administered at the rate of 1 ml. per 20 seconds, the quantity required to reach the stage at which questions were not answered varied from 1.5 to 4.5 ml.; quantities required for surgical anaesthesia varied from 2 ml. to more than 10 ml. Induction was smooth and pleasant. Respiratory depression was more marked than with Evipan sodium, but recovery is more rapid than with any other barbiturate. Its administration requires constant attention and care must be taken not to inject it into the tissues.—O. J. Murphy, *Brit. med. J.*, ii/1936, 1308.

Pentothal is probably the most powerful barbiturate yet produced. In experienced hands it seems to be quite as safe as Evipan, and is certainly a great deal safer than chloroform and its mixtures. Used with care in the selection of cases and technique of administration, there can be no possible doubt that it is one of the most valuable advances in the science of anaesthesia that has been made in recent times.—F. B. Mallinson, *Lancet*, ii/1937, 1070.

Pentothal given intravenously has gradually gained ground at the expense of Evipan. Its use results in an extremely smooth and pleasant induction to anaesthesia, marked relaxation and freedom from the muscular twitching occasionally seen with Evipan. If Pentothal is injected rapidly the desired depth of anaesthesia can be attained by a smaller dose than if it were given slowly. The rapid injection method is used with advantage in two groups of cases, (a) for orthopaedic manipulation in which transient deep anaesthesia is required, and (b) in dentistry. If Pentothal 0.15 to 0.2 g. is injected rapidly an average adult will lose consciousness, allowing for the patient to be given nitrous oxide without his knowledge.—R. R. Macintosh, *Practitioner*, ii/1939, 539.

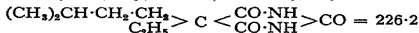
With careful administration respiratory depression is rare. Post-anaesthetic

headache, nausea and vomiting are rare, and the fall in blood pressure is minimal. Sloughing of tissue and irritation at the site of injection may be prevented by the injection of a 2.5% solution and a maximum dose of 1 g. seldom needs to be exceeded. The injection must be given slowly, taking from 1 to 2 minutes.—H. S. Ruth *et al.*, *J. Amer. med. Ass.*, ii/1939, 1864.

Thrombosis following intravenous injection of 0.5 g. of a 5% solution.—F. Evans, *Lancet*, ii/1939, 252.

**FRACTURES.** The ideal anaesthetic for use in the reduction of fractures in ambulatory patients, because it produces sufficient muscular relaxation for reduction, can be continued as long as necessary, has short induction and emergence times, is easily administered and has an adequate margin of safety with few contraindications. It is the agent of choice in fractures with an associated head injury.—P. S. Marcus, *New Engl. J. Med.*, i/1940, 137.

[P1-S1-S4] **Amytal** (Lilly, London) is isoamylethylbarbituric acid,



Supplied in tablets containing  $1\frac{1}{2}$  or  $\frac{3}{4}$  gr., also in crystal form.

A white, crystalline powder, with slightly bitter taste; **soluble** in alcohol and ether; very slightly in water; insoluble in paraffin hydrocarbons. M.p.  $153^\circ$  to  $155^\circ$ . Saturated aqueous solutions are acid to litmus.

**Dose.**—As sedative,  $\frac{1}{2}$  to  $\frac{3}{4}$  grain (0.02 to 0.04 g.) at 2-hour to 4-hour intervals, with water or hot milk. As hypnotic,  $1\frac{1}{2}$  to 5 grains (0.1 to 0.3 g.), 1 to  $1\frac{1}{2}$  hours before retiring. As local or general anaesthetic, 3 to 10 grains (0.2 to 0.6 g.) according to age, etc. As antispasmodic in tetanus to control convulsions, 6 to 12 grains (0.4 to 0.8 g.).

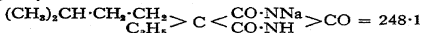
**Uses.** A sedative and hypnotic in the control of insomnia and as a preliminary to surgical anaesthesia. It is stated not to be excreted in the urine and not to affect the kidneys. It also exerts an antispasmodic action and has been employed in the treatment of various types of convulsions of nervous origin and in acute cocaine poisoning.

A hypnotic rather than a true anaesthetic. May be combined with spinal anaesthesia.—J. T. Mason and J. E. Baker, *Lancet*, i/1930, 1302.

In obstetrics, 30 mg. per kilo body weight per rectum produces effective anaesthesia and amnesia, with little, if any, effect on the baby.—D. L. Drabkin, *J. Amer. med. Ass.*, ii/1929, 1175; see also *ibid.*, 1339.

[P1-S1-S4] **Amytal Compound** (Lilly, London). Capsules containing amytal  $1\frac{1}{2}$  gr. and amidopyrine  $3\frac{1}{2}$  gr. Sedative and analgesic.

[P1-S1-S4] **Sodium Amytal** (Lilly, London) is the sodium salt of isoamylethylbarbituric acid.



Supplied in capsules containing 1 gr. or 3 gr., and in ampoules containing 0.125, 0.25, 0.5 or 1 g.

This ureide is isomeric with Nembutal. It is a white, friable, hygroscopic, odourless, granular powder with slightly bitter taste; very **soluble** in water, about 1 in 1 of alcohol 90%, and practically insoluble in ether.

**Dose.**—As sedative or hypnotic in capsules containing 3 grains

(0.2 g.), *per os*, repeated if necessary at 6-hour intervals. As antispasmodic in tetanus, 6 to 12 grains (0.4 to 0.8 g.) to control convulsions.

It is also given by the following methods:

**Rectally** not exceeding 15 grains (1 g.), with a maximum of 1.5 g. in 3% aqueous solution, followed immediately by injection of 1 or 2 ounces of water.

**Intravenously** has been given in dose of 5 to 15 grains (0.3 to 1 g.) in 10% solution at rate of 1 ml. per minute. Blood pressure has to be watched continuously. There are many contraindications, and should only be given by this route when oral administration is not feasible.

**Intramuscularly** not more than 5 ml. of 10% solution should be injected at any one point.

As a pre-anæsthetic the dose is from 3 to 10 grains (0.2 to 0.6 g.)—but only safe for use for this purpose (and in tetanus) by experienced workers familiar with the literature.

**Uses.** Primarily, as hypnotic for basal narcosis. Also as general hypnotic and in obstetrics, and as an antispasmodic in the treatment of tetanus.

Average fatal dose orally for dogs 125 mg. per kilo; rectally and intravenously in 10% solution, 200 and 70-75 mg. per kilo respectively.—E. E. Swanson and H. A. Shonle, *J. Pharmacol.*, Feb., 1931, 305.

Causes marked drop in blood pressure intravenously. Unconsciousness lasts 3 to 6 hours. Safer *per os* or *per rectum*. In medicine, useful for the control of convulsions in unmanageable cases and as a specific for strychnine poisoning (extensive American bibliography).—L. G. Zervas, *Brit. med. J.*, ii/1930, 897; *Lancet*, ii/1930, 693.

Risk of insufficient pulmonary ventilation in period of sleep (24-48 hours) after operation, and a large number require catheterisation.—J. T. Mason and J. E. Baker, *per Lancet*, i/1930, 1302.

**LABOUR.** Best procedure in women of average weight  $\frac{1}{2}$  to  $\frac{3}{4}$  gr. of morphine,  $\frac{1}{16}$  to  $\frac{1}{8}$  gr. of scopolamine, and 6 to 9 gr. of Sodium Amytal intramuscularly, when contractions are regular and occurring at less than 10-minute intervals—injections repeated as indicated. Intravenous injections given at beginning of second stage of 6 to 10 gr. during several pains, and stopped when patient is well controlled. Rapid in action and has a wide range of safe dosage. No harm to mother and labour not delayed.—A. R. Robbins, *J. Amer. med. Ass.*, ii/1929, 1251.

Amytal and Sodium Amytal as analgesics in confinements. 3 grains at first, late in first stage of labour. If necessary repeat in 4 hours.—*Lancet*, ii/1930, 1086.

Sodium Amytal in labour not well spoken of. Morphine and nitrous oxide or rectal Avertin in preference.—J. Riddell, *Lancet*, i/1931, 162.

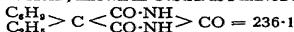
Some patients can take enormous doses of Sodium Amytal ingested orally. One patient was taking 30 capsules a day of the 3 grain capsules. She could not go on without it and, if suddenly deprived of it, suffered from severe convulsions. This patient was incoherent in speech and inco-ordinate in her muscular actions; her face was so changed from its normal expression that she looked like a wild idiotic type of person, although normally of a fine character. This patient was deprived of her drug, has remained free from it, and is living a happy, normal life.—A. Lambert, *New Engl. J. Med.*, ii/1936, 74.

**Benzedrine sulphate** is effective in preventing or counteracting the narcosis produced by the intravenous administration of Sodium Amytal. This action, and the fact that Benzedrine sulphate causes a rapid and prolonged rise in blood pressure, may be found useful in certain medical or surgical cases in which it seems desirable to overcome severe side effects of the narcosis produced by the barbiturates, particularly respiratory embarrassment and pronounced decrease in blood pressure.—A. Myerson *et al.*, *New Engl. J. Med.*, ii/1939, 1015.

[P1-S1-84] **Venesetic** (*Parke, Davis, London*). Sodiumisoamylethylthiobarbiturate in dry ampoules containing 1.5 g. with 20 ml. ampoules of sterile water. For intravenous anaesthesia. Anaesthesia occurs in 20 to 60 seconds and lasts for 20 to 30 minutes.

It is employed by intravenous injection as a short-acting barbiturate for basal narcosis immediately preceding general anaesthesia, or as a complete anaesthetic for short operations when given in repeated doses. A freshly prepared 7.5% solution in distilled water (1.5 g. in 20 ml.) is injected intravenously in exactly the same way and observing the same precautions as in the case of Evipan sodium and Pentothal sodium, and it would appear that the results are almost indistinguishable from those obtained with the latter preparations.—C. Langton Hewer (Therapeutic Trials Committee), *Brit. med. J.*, i/1939, 109.

[P1-S1-84] **Phanodorm** (*Bayer Products, London*). CYCLOHEXYN-ETHYLBARBITURIC ACID; known in U.S.A. as PHANODORN.



**Dose.**—Average dose 1 tablet (3 grains). In mild insomnia, 1½ grains; obstinate insomnia, 3 to 6 grains. Larger dose not repeated in less than 12 hours.

A white, crystalline powder, with bitter taste; **soluble** in alcohol and ether, only slightly soluble in water.

**Uses.** Sedative in nervous conditions and insomnia. In nerve affections to be taken in warm water. Is stated to be more rapidly eliminated than barbitone, and hence its action is of shorter duration.

[P1-S1-84] **Phanodorm Calcium** (*Bayer Products, London*). Tablets containing Phanodorm and calcium. **Dose.**—As for Phanodorm.

[P1-S1-84] **Hebaryl Sodium** (*Parke, Davis, London*). Known as Ortol-Sodium in U.S.A. The sodium salt of normal hexylethyl barbituric acid. **Average dose.**—1 to 2 capsules of 3 grains each. Hypnotic and sedative.

[P1-S1-84] **Hexobarbitonum** (*B.P. Add. III*). **Syn. and Prop. Names.** HEXOBARBITAL, METHEXENYL, HEXANASTAB-ORAL (*Boots, Nottingham*), EVIPAN (*Bayer Products, London*); known in U.S.A. as EVIPAL.



**Dose.**—4 to 8 grains (0.25 to 0.5 g.).

Hexobarbitone is 5-Δ<sup>1</sup>-cyclohexenyl-5-methyl-N-methylbarbituric acid, occurring as a colourless, crystalline, odourless powder with a slightly bitter taste; m.p. 145° to 147°.

Sparingly **soluble** in water, but soluble in alcohol, acetone and other organic solvents; also soluble in alkali hydroxides, but not in solutions of alkali carbonates.

**Uses.** A rapidly absorbed hypnotic with immediate intensive action of short duration. It is employed for the relief of insomnia not due to pain, sleep following within ten minutes of administration. It is rapidly excreted and is said to be free from habit formation.

[P1-S1-84] **Hexobarbitonum Solubile** (*B.P. Add. III*). **Syn. and Prop. Names.** SOLUBLE HEXOBARBITAL, METHEXENYL SODIUM, CYCLONAL SODIUM (*Pharmaceutical Specialities (May & Baker)*)

*Ltd., London*), EVIPAN SODIUM (*Bayer Products, London*), HEXANASTAB (*Boots, Nottingham*).

**Dose.**—3 to 15 grains (0.2 to 1 g.), as a 10% solution, for intravenous or intramuscular injection;  $\frac{1}{2}$  to 1 drachm (2 to 4 g.), *per rectum*.

Soluble hexobarbitone is the mono-sodium salt of hexobarbitone, occurring as a white, odourless, very hygroscopic powder.

Readily **soluble** in water, alcohol and acetone; slightly soluble in chloroform and ether; insoluble in benzene. The aqueous solution is not stable for more than two or three hours and should be freshly prepared before use, since it absorbs carbon dioxide from the air with the deposition of hexobarbitone. Before use it is important to ensure that the powder is completely dissolved and the resulting solution clear.

**Toxic Effects.** Muscular twitchings of the arms and face, and sometimes extending over the whole body, are of fairly frequent occurrence; premedication with morphine and scopolamine tends to prevent their occurrence. Respiratory depression occurs during operation; this is usually only temporary, but fatal respiratory failure has occurred in a few cases. In cases of collapse following administration an injection of from 5 to 10 ml. of nikethamide is of value. Excitement or restlessness after operation is sometimes a cause of trouble and occasionally a dose of morphine may be found necessary. Apparent overdose or delayed recovery is best treated by an intravenous injection of 2 ml. of a 0.3% solution of picrotoxin.

Details of 6 fatalities.—G. Slot and A. H. Galley, *Brit. med. J.*, ii/1934, 204.

A case of late paralysis due to Evipan administration.—J. V. Landon and M. Salleh, *Brit. med. J.*, ii/1934, 940. See also F. B. Mallinson, *ibid.*, 1025.

Most authorities lay stress on the advisability of slow injection.—J. Blomfield, *Med. Annu.*, 1935, 21.

Preliminary Report of the Council on Pharmacy and Chemistry of the A.M.A.—Evipal soluble (Evipan sodium) was introduced as a general anæsthetic to be injected intravenously before adequate studies had been made of it under a great variety of conditions. It probably has a narrow field of usefulness in which it may be employed with relative safety, provided it is used with skill and with due regard for its limitations. It is believed that the anæsthetic is wholly or partly responsible for forty-three deaths (listed in the report), though several of these would have occurred with any anæsthetic, and in the absence of any.—*J. Amer. med. Ass.*, i/1937, 1172.

**Contraindications.** It should not be employed in patients with impaired liver function, in acute inflammatory conditions of the respiratory tract or where any respiratory obstruction exists or may arise; its use is not advisable in patients with asthma. It is also contraindicated in advanced cardiac disease, in septicæmia, and in the presence of general debility and low blood pressure. It should be used with care in patients with diseases of the central nervous system, and its employment is not advised in old and feeble persons.

**Uses.** Soluble hexobarbitone is a convenient anæsthetic for surgical and dental operations of short duration. Its action is remarkably evanescent, consciousness returning within ten to twenty minutes after administration of a full dose. It may be used

either alone or as a preliminary to an inhalation anaesthetic, and is usually employed by intravenous injection, though it has also been used intramuscularly and *per rectum*. With the patient lying down the solution should be introduced slowly into the vein through a small needle. Injection at the rate of 1 ml. in 3 seconds is made of 2.5 or 3 ml.; this is followed by a pause of 30 seconds; if unconsciousness follows this will last for 2 to 3 minutes, but if unconsciousness does not follow 2 or 3 more ml. are injected, and anaesthesia should then last for 5 minutes; for anaesthesia lasting 10 to 20 minutes, from 5 to 7 ml. are given without a pause. A single dose of 10 ml. should never be exceeded. It should never be administered single-handed nor to patients in the upright position.

In addition to its use in surgery, soluble hexobarbitone has also been employed for the relief of pain in childbirth, and has been used with success in the treatment of tetanus and cocaine poisoning.

A method of minimising respiratory depression when using soluble barbiturates (e.g., Evipan or Nembutal) intravenously, by the incorporation of a respiratory stimulant in the same solution with the anaesthetic. Starting with a solution of the barbiturate, made so that each 1 ml. of the solution contains 100 mg. of barbiturate, 25 mg. of the stimulant (Coramine) is added to each 1 ml. of the solution. The needle is kept in the vein throughout the operation, and the same principle of intermittent administration is utilised as is employed in the semi-open method of administration of ethyl ether. To ensure that respiratory exchange is taking place a fluffy piece of cotton is fastened to the upper lip by a narrow piece of adhesive tape. Patency of the airway must be maintained by sustaining the lower jaw. Encouraging results obtained.—J. S. Lundy, *Proc. Mayo Clin.*, 1935, 791.

A splendid addition to anaesthetics if we realise its limitations, and that what is gained by steadiness of anaesthesia may be lost by restricted flexibility. It is a light anaesthetic, having the advantage of ease of induction over gas and oxygen, but it is doubtful if it is really better than the older methods, and in the case of really extensive operations there are no advantages. It is now recognised that its use should be restricted to those with a sound knowledge of drugs and general anaesthetic routine, and its simplicity should not tempt the operator to give his own injections. All the advantages may be offset by chest complications caused by respiration depression, and occasionally there is excitement necessitating supervision for many hours, while the stupor which sometimes follows makes it difficult to judge as to the rallying of the patient, thus making excessive demands upon the nurses, as the patient must be watched continuously to avoid obstruction of the breathing.—H. T. Roper-Hall, *Proc. R. Soc. Med.*, Jan., 1936, 276.

**DELIRIUM TREMENS.** The intravenous injection of 2 ml. of a 10% solution produced striking effects in three cases. The patients suddenly stopped struggling and relaxed, and then dropped into a deep sleep. A further injection of 1 ml. was then given. The pulse and respiration rates returned to normal and sweating ceased. Sleep lasted for 18 to 24 hours and the patients woke free from delirium and with no recollection of it.—P. Sperber, *New Engl. J. Med.*, 1/1937, 1065.

**Rectal Anaesthesia.** Evipan sodium was successfully employed *per rectum* as a basal anaesthetic in 518 cases. The patient receives 0.2 ml. of a 10% aqueous solution per pound body weight, i.e., a total of 30 ml. for a man weighing 150 lbs. A preliminary enema of sodium bicarbonate is given two hours before administration; no soap-suds enema is required. From 40 to 60 minutes before the Evipan sodium is administered morphine or Dilaudid is injected hypodermically. The solution of Evipan is prepared by dissolving 3 g. in 30 ml. of distilled water which is then drawn into a 30 ml. glass syringe with a very small catheter attached, the calibre fitting the syringe exactly. The entire contents of the syringe are then rapidly injected and the catheter clamped and left *in situ* until the patient falls asleep. It is a practical and satisfactory method, eliminating the dangers inherent

in intravenous use. In none of the cases was there any untoward symptoms during operation, and in only 2% was there post-operative excitement.—A. E. Jones, *J. Amer. med. Ass.*, i/1938, 1419.

[P1-S1-S4] **Narconumal** (*Roche Products, Welwyn Garden City*).  $C_{11}H_{15}O_3N_2Na = 229.2$ .

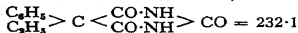
**Dose.**—5 to 30 grains (0.3 to 2 g.) as a 10% solution for intravenous injection.

The sodium salt of 1-methyl-5:5-allylisopropylbarbituric acid, supplied in 1 g. ampoules together with 10 ml. ampoules of distilled water.

**Contraindications** are the same as those for soluble hexobarbitone.

**Uses.** As a basal hypnotic for the induction of anæsthesia, or for producing full surgical anæsthesia of long or short duration. The patient should be prepared as for an inhalation anæsthetic. As a basal narcotic up to 10 ml. of a 10% solution is given intravenously, the anæsthesia being completed with ether or gas and oxygen followed by ether. For the induction of short anæsthesia from 4 to 5 ml. is injected in four to five minutes, followed by a pause of 30 seconds, and then by the injection of 2 ml. per minute up to an average of 7 ml. for women and 9 ml. for men. For prolonged anæsthesia 11 ml. is injected during the first 15 minutes and then a maintenance dose of 2 ml. every quarter of an hour up to a total of 20 ml. if required. The recovery period is from 20 to 25 minutes after a dose of 4 ml. and about 1½ hours after a dose of 8 to 10 ml. After returning to bed an airway must be maintained until full consciousness returns, and the patient must not be left unattended.

[P1-S1-S4] **Phenobarbitonum** (*B.P.*). *Syn. and Prop. Names.* 5-PHENYL-5-ETHYLBARBITURIC ACID, PHENYLETHYLMALONYL UREA (*Fr. Cx.*), PHENOBARBITALUM (*U.S.P. XI, P. Helv. V, P. Jap. V*), ACIDUM PHENYL-ÆTHYLICOBARBITURICUM (*P. Ned. V, P.G. VI, P. Svec. X, F.E. VIII, P. Dan.*), LUMINAL (*Bayer Products, London*), GARDENAL (*Pharmaceutical Specialities (May & Baker) Ltd., London*), SOMONAL (*Richter, London*).



**NOTE.**—The name "Barbitone" is applied in error in *Fr. Cx.* as a synonym for Phenobarbitone.

**Dose.**—½ to 2 grains (0.03 to 0.12 g.). More is sometimes given; where there is much excitement, 5 to 6 grains up to 12 grains (0.8 g.), the maximum dose as given in *P. Belg.*; *U.S.P. XI*, average dose ½ grain. *Fr. Cx.* has maximum single dose 3 grains, maximum in 24 hours 7½ grains.

A white powder, melting at 173° to 177°.

**Soluble** about 1 in 1000 of water, 1 in 15 of alcohol 90%, 1 in 40 of ether, 1 in 50 of chloroform. Readily soluble in aqueous alkali hydroxides and carbonates.



**Toxic Effects.** These are similar to those produced by barbitone, the most common symptom of intoxication being the formation of a rash, especially where there is an idiosyncrasy to the drug.

The treatment of acute poisoning is the same as for barbitone.

A patient who had taken 18 gr. of Amytal and 60 gr. of phenobarbitone failed to respond to strychnine in convulsive doses. A voluntary motion of the head was made after the first injection of picrotoxin (dose not stated), and uneventful recovery followed the injection of a total of 131 mg. of picrotoxin during 48 hours.—S. J. Cohen and R. Kohn, *J. Pharmacol.*, 1937, 60, 102.

**Contraindications.** Pulmonary and cardiac disease, arteriosclerosis, nephritis and parkinsonism.

Phenobarbitone and probably other barbiturates are contraindicated in parkinsonism; they cause a marked aggravation of the rigidity.—E. and E. S. Ziskind, *J. Amer. med. Ass.*, ii/1937, 20.

**Uses.** Phenobarbitone and soluble phenobarbitone are employed for their hypnotic and sedative action. They have a greater intensity of action than barbitone and a smaller margin of safety. The range of uses is similar to that of barbitone except that phenobarbitone is used more especially in the treatment of epilepsy, though tolerance may follow its prolonged use in these cases.

EPILEPSY treated by Luminal. Doubtful whether 5 or 6 grains should be exceeded as a single dose *per os*. Rashes and poisoning symptoms—headaches, vertigo, lethargy, etc. Also of use in migraine, insomnia (1 to 1½ grains at bedtime), aural vertigo. Recurrent attacks well treated. Also in cutaneous affections with a neurotic factor.—W. Russell Brain, *Lancet*, ii/1929, 867.

At the David Lewis Colony, treatment is instituted with 2 gr. of soluble phenobarbitone dissolved in ½ oz. of water and given each morning. At the end of 2 weeks any nausea or sleeplessness should have disappeared. The case is reviewed at the end of a month and appropriate alterations made (e.g., alteration of dose, time of giving, etc.). The drug may be stopped at the end of 6 months if no change has been produced or is expected. Administration is safe over long periods. In 1933 over 400 patients were taking the drug regularly: some had taken it daily for more than 12 years. No knowledge of a single case of phenobarbitone addiction in an epileptic, and no instance of Luminal skin rash has been observed.—R. Handley, *J. ment. Sci.*, 1934, 80, 526.

**PAINFUL CONDITIONS.** Hypodermic injection of 1½ grains effective in severe pain, such as tabetic crises and herpes zoster. Relief in 20 to 30 minutes.—L. Gunther and H. M. F. Behneman, *per J. Amer. med. Ass.*, ii/1928, 832.

**VOMITING OF PREGNANCY** completely controlled by ½ to 1 grain of Luminal nightly, but tends to recur if drug is omitted. Non-toxic in this dose over long periods.—A. Elliott, *Brit. med. J.*, ii/1931, 1119.

**WHOOPING COUGH.** To control the severity of paroxysms which are threatening life by their mechanical violence or by imminent secondary complications, Luminal Sodium is of proved value. In the presence of vomiting, the amount of drug administered by the mouth is probably not absorbed, but two or three doses given intramuscularly appear to act as a specific in checking the vomiting, when oral administration may be resumed. Careful adjustment of dosage to bodyweight, and constant observation of its action in controlling the spasms short of producing undue somnolence, make it a valuable therapeutic weapon apparently free from risk even in infants.—William Gunn, *Practitioner*, ii/1936, 521.

[P1-81-84] **Elixir Phenobarbitoni (B.P.C.).**

**Dose.**—1 to 2 drachms (4 to 8 ml.).

A flavoured preparation containing ½ gr. of phenobarbitone per drachm (0.5%) and coloured yellow. To avoid waste the quantities of each of the volatile oils should be reduced by 25%.

[P1·81·84] **Elixir Phenobarbitali** (N.F. VI) contains 0·4% of phenobarbital, and coloured red.

[P1·81·84] **Tabellæ Phenobarbitoni** (B.P.C.) contain  $\frac{1}{2}$  gr. (0·03 g.).

[P1·81·84] **Tabellæ Phenobarbitoni et Theobrominæ** (B.P.C.). *Prop. Names.* TAB. XANTHARBIN (*Thackray, Leeds*), THEOBA (*Burroughs Wellcome, London*), THEOGARDENAL TABLETS (*Pharmaceutical Specialities (May & Baker) Ltd., London*), THEOTONE TABLETS (*Allen & Hanburys, London*), THEOMINAL TABLETS (*Bayer Products, London*).

*Dose.*—1 or 2 tablets.

Phenobarbitone  $\frac{1}{2}$  gr. and theobromine 5 gr. For high blood pressure, angina pectoris and menopausal disorders.

[P1·81·84] **Alepsal** (*Genetrier, Neuilly; Wilcox, Jozeau, London*). Tablets containing phenobarbitone  $1\frac{1}{2}$  gr., powdered belladonna  $\frac{1}{8}$  gr., and caffeine  $\frac{1}{2}$  gr. Also issued in medium and weak strengths. In epilepsy, migraine and spasmodic affections.

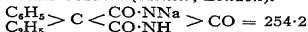
[P1·81·84] **Cafinal** (*Bayer Products, London*). Tablets of Luminal  $\frac{1}{2}$  gr., and caffeine  $\frac{1}{2}$  gr. *Dose.*—1 to 3 tablets daily. In migraine, epilepsy, dysmenorrhœa, etc. [P1·81·84] **Cafinal Compound** tablets, containing Cafinal with scopalamine hydrobromide, ephedrine, papaverine hydrochloride, atropine methylobromide and strychnine nitrate. For travel sickness. *Dose.*—3 half an hour before starting.

[P1·81·84] **Optinoktin** (*Richter, London*). Phenobarbitone 0·1 g., bromoisovalerylurea 0·2 g., amidopyrine 0·2 g. *Dose.*—1 or 2 tablets nightly. Neuralgia, migraine, etc.

[P1·81·84] **Nulepsi** (formerly known as **Salepsi**) (*Coates & Cooper, London*). Each pill contains phenobarbitone 0·05 g., solanaceous alkaloids 0·00005 g., cascara sagrada 0·1 g., valerian 0·04 g. *Dose.*—1 to 4 daily. Also available in solution. For epilepsy.

[P1·81·84] **Theobromal** (*Richter, London*). Tablets contain theobromine calcium salicylate  $4\frac{1}{2}$  gr., phenobarbitone  $\frac{1}{2}$  gr. *Dose.*—1 tablet three times daily. Hypertension, angina pectoris.

[P1·81·84] **Phenobarbitonum Solubile** (B.P., P.G. VI, P. Ned. V *Supp. II*, P. *Helv. V*, P. *Svec. X*, P. *Dan.*). *Syn.* SODIUM PHENOBARBITONE, PHENOBARBITALUM SOLUBILE (U.S.P. XI, P. *Helv. V*, P. *Jap. V*), GARDENAL-SODIUM (*Pharmaceutical Specialities (May & Baker) Ltd., London*), LUMINAL-SODIUM (*Bayer Products, London*), SOMONAL SODIUM (*Richter, London*).



*Dose.*— $\frac{1}{2}$  to 2 grains (0·03 to 0·12 g.). It has also been given hypodermically in doses of  $\frac{1}{2}$  to 3 grains (0·03 to 0·2 g.) daily in 20% solution, e.g., in epilepsy. P.G. VI states max. single dose 6 grains, max. daily dose 12 grains; P. *Helv. V* has 3 and 5 grains approx. respectively.

It is the mono-sodium derivative of phenobarbitone, and occurs as a white hygroscopic powder with bitter taste.

**Soluble** readily in cold water and in alcohol 90%; insoluble in ether or chloroform. Aqueous solutions should be freshly prepared with recently boiled and cooled water.

**Incompatible** with ammonium salts as they decompose quickly, also with acids and acidic substances which precipitate phenobarbitone. In preference give it alone. Solutions should not be

heated, since phenylethylacetylurea is precipitated. The same decomposition may occur on long standing.

**DECOMPOSITION IN AQUEOUS SOLUTION.** Soluble phenobarbitone slowly hydrolyses in solution with production of  $\text{CO}_2$  and a precipitate of phenylethylacetylurea. A 10% solution (pH 9.4) decomposes only to the extent of 1% at 20° in three weeks. The more strongly alkaline solutions decompose somewhat more rapidly than those containing less alkali.—L. Nielsen, *Dansk. Tidsskr. Farm.*, 1933, 7, 137.

**PHENOBARBITONE SOLUTION FOR INJECTION.** The instability and alkalinity of solutions of soluble phenobarbitone make it unsuitable for injection. The following solution has been found satisfactory:—Phenobarbitone 20 g., amylene hydrate 38 g., ethyl urethane 35 g., water 7 ml. Sterilise by filtration using pressure rather than suction in order to avoid evaporation.—E. V. Christensen, *Arch. Pharm. Chem.*, 1932, 89, 529.

An aqueous solution of soluble phenobarbitone is unstable, but the following solution can be heated to 80° to 65° for 30 minutes on two successive days without any appreciable decomposition occurring. Phenobarbitone 10 g., diethylamine 2.75 g.; dissolve and add a sufficient quantity of a mixture containing alcohol 26 g., glycerin 31 g. and water to 100 ml., to produce a 5% or 20% solution.—C. J. Blok, *Pharm. Weekbl.*, 1935, 1221.

Phenobarbitone 3.0 g., soluble phenobarbitone 6.72 g., urethane 2.5 g., alcohol 95% 15 g., glycerin 12.5 g., water to 100 ml. In 3 months at 12° only 0.55% of the phenobarbitone decomposes, the loss being only  $\frac{1}{2}$  that in aqueous solutions. If sterilised at 80° for 2 hours the loss is about 0.75%. No precipitation of phenylethylacetylcarbamide occurs until the decomposition amounts to 12%.—L. Nielsen, *Dansk. Tidsskr. Farm.*, 1937, 65.

[P1-S1-84] **Mistura Phenobarbitoni** (*Gt. Orm. H.*). (Dose for 1 year old child). Soluble phenobarbitone  $\frac{1}{2}$  gr., potassium bromide 2 gr., elixir of gluside  $\frac{1}{2}$  m., chloroform water to 1 dr.

[P1-S1-84] **Tabellæ Phenobarbitoni Solubilis** (*B.P.C.*). Contain  $\frac{1}{2}$  gr. (0.03 g.).

[P1-S1-84] **Elixir Phenobarbital Co.** (*Duncan, Flockhart, Edinburgh*). Each fl. dr. contains soluble phenobarbitone  $\frac{1}{2}$  gr., potassium bromide 5 gr. *Dose*.—1 to 2 fluid drachms. Hypnotic and sedative.

[P1-S1-84] **Epilamin** (*Richter, London*). Tablets containing sodium phenobarbitone  $\frac{1}{2}$  gr., potassium bromide 10 gr., calcium glycerophosphate  $\frac{1}{2}$  gr., calcium formate 3 gr., vitamin D 300 units. *Dose*.—1 to 5 tablets daily. Epilepsy.

[P1-S1-84] **Lubrokral** (*Coates & Cooper, London*). Tablets of potassium bromide 9 gr. and soluble phenobarbitone  $\frac{1}{2}$  gr. *Dose*.—1 tablet 3 times daily. Convulsions and nervous insomnia.

[P1-S1-84] **Phemitonum** (*B.P. Add. III*). *Prop. Name*. PROMINAL (*Bayer Products, London*).  $\text{C}_{13}\text{H}_{14}\text{O}_3\text{N}_2 = 246.1$ .

*Dose*.— $\frac{1}{2}$  to 6 grains (0.03 to 0.4 g.).

N-methyl-5-phenyl-5-ethylbarbituric acid, occurring as a white, crystalline powder; m.p. 178° to 181°.

Almost *insoluble* in cold water, but freely soluble in hot water; also soluble in organic solvents and alkali hydroxides.

**Uses.** Anti-epileptic and spasmodic with hypnotic action.

**EPILEPSY.** Led to a striking reduction in the incidence of fits in 10 cases and patients were more bright, cheerful and contented. In four cases Prominal was substituted for Luminal with improved results. The usual dose was 3 grains once or twice daily. A daily dose showed no cumulative effect.—L. G. M. Page, *Brit. med. J.*, i/1936, 531. Results corroborated in four cases.—L. Barber, *ibid.*, 666.

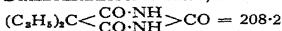
Experience with 39 mentally defective epileptics showed that the frequency of fits while patients were under treatment with Prominal was only one-third the frequency during treatment with Luminal. Dosage was adjusted to individual requirements, adults usually receiving 3 gr. three times a day, which can be taken without ill effects for long periods. A large proportion of cases showed improvement in the non-convulsive manifestations of epilepsy.—C. Guy Millman, *Brit. med. J.*, ii/1937, 61; see also *ibid.*, 63.

[P1-81-84] **Protheonal** (*Bayer Products, London*). Tablets containing Prominal 1 gr., theobromine  $7\frac{1}{2}$  gr., and iodo-calcium-triethanolamine  $2\frac{1}{2}$  gr. equivalent to  $1\frac{1}{2}$  gr. of iodine. For raised blood-pressure, arteriosclerosis, angina pectoris and menopausal vasomotor symptoms. *Dose*.— $\frac{1}{2}$  to 1 tablet three times a day.

[P1-81-84] **Phenylmethylbarbituric Acid** (*P. Ned. V Supp. II*). *Prop. Name* RUTONAL (*Pharmaceutical Specialities (May & Baker) Ltd., London*). A white, crystalline powder, slightly soluble in water and soluble 1 in 54 of alcohol. *M.p.* 226°.

*Dose*.—On the first day one 3-grain tablet in the morning and one at night to test the patient's tolerance, increasing to 4 or 5 tablets in 24 hours. Hypnotic and sedative; specially indicated in epilepsy.

[P1-81-84] **Allobarbitonum** (*B.P.C.*). *Syn.* ALLOBARBITALUM (*P. Helv. V*), 5:5-DIALLYLBARBITURIC ACID, DIALLYLMALONYLUREA.



*Dose*.— $\frac{1}{2}$  to 3 grains (0.03 to 0.18 g.). *P. Helv. V* has max. single dose 3 grains, max. in 24 hours 5 grains.

A white, odourless, crystalline powder with a slightly bitter taste. *M.p.* 171° to 172°. Prepared by the condensation of ethyl diallylmalonate with urea.

**Soluble** in alcohol and ether, and in alkaline solutions; slightly soluble in water.

**Uses.** A sedative and hypnotic for nervous insomnia and to induce narcosis in conditions of severe agitation. It is said to be more readily absorbed than barbitone. Death may be caused by 30 gr., but the average fatal dose is more than double this quantity. Idiosyncrasy, with a rash and fever, may occur.

[P1-81-84] **Cibalgin** (*Ciba, Horsham*).

A compound of amidopyrine with Dial (0.25 g. = 0.22 g. of amidopyrine and 0.03 g. of Dial).

Tablets 4 grains (0.25 g.): *Dose*.—1 to 4. Liquid for oral use, 1 ml. contains Cibalgin 0.25 g. (4 grains), urethane 0.28 g. ( $4\frac{1}{2}$  grains), monoethylurea 0.28 g. ( $4\frac{1}{2}$  grains): *Dose*.—1 to 4 ml. Also supplied in ampoules each containing 2.3 ml. of liquid: *Dose*.— $\frac{1}{2}$  or 1 ampoule daily. The tablets and liquid should be taken with a little warm water or tea, but not in coffee. In neuralgia, migraine, and other types of pain, *e.g.*, dysmenorrhœa, articular and muscular pain.

[P1-81-84] **Dial** (*Ciba, Horsham*). Allobarbitone, supplied in tablets, each containing  $1\frac{1}{2}$  grains (0.1 g.). Liquid for oral use; 1 ml. contains Dial  $1\frac{1}{2}$  grains (0.1 g.), urethane 6 grains (0.4 g.), and monoethylurea 6 grains (0.4 g.). Also supplied in ampoules each containing 2.3 ml. of the liquid.

[P1-81-84] **Dialacetin** (*Ciba, Horsham*). Tablets contain 4 gr. of allyl-*p*-acetamino-phenol and  $1\frac{1}{2}$  gr. of Dial. For use as combined hypnotic, analgesic and antipyretic. *Dose*.—As hypnotic, 1 to 2 tablets with hot drink one hour before bedtime. As sedative,  $\frac{1}{2}$  to 1 tablet one to three times a day.

Nocturnal fits in epilepsy often respond to this ( $\frac{1}{2}$  to 1 tablet at night, or twice daily) when other remedies fail.

[P1-81-84] **Didial** (*Ciba, Horsham*). Tablets contain  $\frac{1}{2}$  gr. of ethylmorphine and  $1\frac{1}{2}$  gr. of Dial. A powerful hypnotic for severe insomnia. *Dose*.—1 tablet. For the induction of "twilight sleep," one to three tablets.

[P1-81-84] **Somnifaine** (*Roche Products, Welwyn Garden City*). A water-glycerin-alcohol solution of the diethylamine salts of diethylbarbituric acid (barbitone) and allylisopropylbarbituric acid, containing the equivalent of 0.1 g. (about  $1\frac{1}{2}$  gr.) of each acid per ml. Available as a flavoured oral solution in drop bottles or in ampoules for injection.

*Dose*.—Orally, 20 to 40 drops (about 8 to 16 m.) 30 minutes before retiring; may be increased up to 60 drops (25 m.). To be taken in water or other vehicle. By injection, 1 ampoule (2 ml.) intramuscularly. In case of urgency, 2 to 3 ampoules by very slow intravenous injection.

**Uses.** A powerful sedative and hypnotic indicated in all conditions of excitement, ravings, or convulsions, in eclampsia, status epilepticus, tetanus, strychnine and cocaine poisoning. Also used in the "twilight sleep" treatment of certain mental disorders.

**PSYCHOSES.** Treatment of psychoses by prolonged narcosis—intramuscular injection of Somnifaine in 2 ml. doses, sufficient to ensure continuous sleep for 10 to 12 days, feeding with fluids being carried out before each injection and at intervals when possible; largest daily dose usually 8 ml. The treatment is dangerous (3 deaths in 60 cases) but often produces definite, and sometimes dramatic, improvement. The concurrent administration of insulin with glucose made for smoother treatment.—D. N. Parfitt, *Lancet*, i/1936, 424.

As this high mortality rate (5%) might well dissuade others from carrying out this valuable form of treatment it should be pointed out that it is not in accord with experience at Cardiff City Mental Hospital. When Somnifaine alone was used there were 2 deaths in 86 treatments (2.3%); but since glucose and insulin have been used to combat toxic symptoms 154 cases have been treated without a single fatality. With careful nursing in a darkened single room, it is rarely found necessary to give more than 4 ml. of Somnifaine in the 24 hours.—P. K. McCowan, *Lancet*, i/1936, 508.

In spite of the attractive theory of disturbed carbohydrate metabolism after Somnifaine, the fact must be faced that the use of insulin in prolonged narcosis is purely empirical. The danger of relying upon insulin as a preventive, and the urinary analysis as an indication of toxæmia, is that the physician may be tempted to neglect that close clinical observation of the patient which is the only efficient safeguard. It cannot be too strongly emphasised that the patient's life may be jeopardised without a trace of acetone appearing in the urine.—D. Menzies, *Lancet*, ii/1937, 713.

**STATUS EPILEPTICUS.** Somnifaine intramuscularly advocated as an efficient remedy. Lumbar puncture and free drainage of spinal fluid, with Sodium Luminal, 6 grains intravenously, also recommended as immediate measures for checking seizures. A 50% solution of magnesium sulphate *per os* cleans alimentary tract and reduces intracranial pressure.—F. McLaughlin, *Practitioner*, ii/1932, 714.

[P1-S1-S4] **Allonal** (*Roche Products, Welwyn Garden City*). A combination of allylisopropylbarbiturate of amidopyrine 0.126 g. (approx. 2 gr.) and amidopyrine 0.034 g. (approx.  $\frac{1}{2}$  gr.), equivalent to about 1 gr. of allylisopropylbarbituric acid and  $1\frac{1}{2}$  gr. of amidopyrine.

**Dose.**—1 to 2 tablets as sedative or hypnotic in simple cases of insomnia, 2 to 4 as analgesic and hypnotic.

2 tablets quickly relieve pain in neuralgia, neuritis, rheumatism, sciatica, etc. Is not habit-forming, and has low toxicity. *Not more than 4 or 5 tablets daily advised until patient's susceptibility is ascertained.*

Death of a woman who had taken 10 tablets a day for more than a year.—*Pharm. J.*, i/1932, 117, 139.

[P1-S1-S4] **Ipral Sodium** (*Squibb, New York; Savory & Moore, London*). Sodium ethylisopropylbarbiturate. A hypnotic and sedative for oral use in pre-anæsthetic medication. **Dose.**—8 gr. (2 tablets) the night before operation and repeated the next morning 2 hours prior to anaesthesia. Also supplied in the form of an elixir. **Ipral-Aspirin Tablets** contain 5 gr. of aspirin and 1 gr. of Ipral, and are employed for the relief of pain and insomnia. **Ipral-Calcium Tablets** 2 gr., are employed as a sedative for ordinary insomnia.

[P1-S1-S4] **Pernocton** (*Riedel-de-Haen, Berlin; Endocrines-Spicer, Watford*). *Syn.* BUTYL- $\beta$ -BROMALLYL-BARBITURIC ACID; known as PERNOSTON in U.S.A.  $C_{11}H_{15}O_3N_2Br = 303.16$ .

Issued in ampoules containing  $3\frac{1}{2}$  grains in 2.2 ml. Average hypnotic dose intravenously 3 ml. (containing  $4\frac{1}{2}$  grains), given

at the rate of 1 ml. per minute. Also available in 5 ml. ampoules, and in tablets containing 3 gr.

Resembles Sodium Amytal in action, but is a more powerful hypnotic. In addition, there is less restlessness during recovery period, and no fall in blood pressure.

**DENTAL WORK.** Pernocton intravenously. A good anæsthetic, conducting operation under gas and oxygen through a Magill tube. Nembutal and Avertin also suitable, but no advantage over Pernocton.—R. R. Macintosh, *Brit. dent. J.*, Feb. 15, 1932.

**MORPHINISM.** A cure obtained in from 4 to 5 days, in the patient's own home, in all but one of 12 cases. Twilight sleep is induced during this period by three injections at 8 a.m., 4 p.m. and midnight, Pernocton 2 ml. intravenously and 2.2 ml. intramuscularly being injected thrice daily. To the intramuscular injection is added 0.002 g. of atropine to obviate the disorders of abstinence. Food in fluid form given prior to each injection, and fruit juice and glucose in between.—L. König, *Med. Klinik*, 1935, 246.

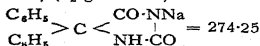
[P1-S1-84] **Sandoptal** (*Sandoz, London*). *iso*Butylallylbarbituric acid. Tablets contain 3 grains. *Dose*.—In simple insomnia 1 tablet; in persistent insomnia 2 tablets.

[P1-S1-84] **Optalidon** (*Sandoz, London*). Sandoptal 0.05 g., amidopyrine 0.125 g., caffeine 0.025 g. *Dose*.—2 tablets several times daily as required. Sedative and hypnotic.

[P1-S1-84] **Noctal** (*Riedel-de-Haen, Berlin; Endocrines-Spicer, Watford*). Known as NOSTAL in U.S.A. *iso*Propylbromallylbarbituric acid. *Dose*.—1 or 2 tablets before retiring. Narcotic and sedative.

[P1-S1-84] **Seconal** (*Lilly, London*). Sodium propylmethylcarbonylallylbarbiturate, a rapidly effective barbiturate with short duration of action. *Dose*.—In the first stage of labour the dose is 3 to 4½ gr. initially, followed by doses of 1½ to 3 gr. at intervals when the pains are severe. For pre-operative medication in surgery, 3 to 4½ gr. ½ to 1 hour before operation. For insomnia 1½ gr. or more as required. Supplied in capsules containing 1½ gr.

**Sodii Diphenylhydantoinas.** *Prop. Names.* DILANTIN SODIUM, EPANUTIN (*Parke, Davis, London*) (1½ gr. capsules), EPTOIN (*Boots, Nottingham*) (1½ gr. capsules), SOLANTOIN (*Glaxo Laboratories, London*) (1½ gr. tablets).



*Dose*.—1½ grains (0.1 g.) two to four times daily.

Sodium diphenylhydantoinate is the sodium salt of 5:5-diphenylhydantoin. It is an odourless, white or cream-coloured powder with a bitter taste.

**Soluble** in water, slightly soluble in alcohol, but insoluble in ether or benzene. In aqueous solution it is hydrolysed to the base, and the latter only dissolves if the reaction of the solution is adjusted to pH 11.7.

**Toxic Effects.** The margin between the therapeutic and the toxic dose is very small and toxic reactions are of not infrequent occurrence; these include dizziness, tremor, ataxia, diplopia, nausea, fever, dermatitis, and swelling of the gums.

**Uses.** An anticonvulsant for use in the treatment of epileptic patients who fail to benefit under barbiturates and bromides. It appears to be more effective in controlling seizures of the grand

mal type than in those of the petit mal. The initial dosage for adults and children over six years of age is  $1\frac{1}{2}$  gr. three times daily. If the seizures are not controlled by this dose in 7 days a further  $1\frac{1}{2}$  gr. should be given at bedtime, and the dose may be further increased, if necessary, up to a maximum of 9 grains in 24 hours. Infants and children up to five should be started on a dose of  $1\frac{1}{2}$  to 3 gr. daily, increased up to  $4\frac{1}{2}$  to 6 gr. daily. If favourable results are not obtained in two or three weeks it is probable that the treatment will not be effective. The drug is more rapidly effective if given before meals, but where it causes gastric irritation it should be given immediately after meals. If the patient is already taking phenobarbitone or bromides, the transition to sodium diphenylhydantoinate should be made gradually, with some overlapping in dosage, thus avoiding the danger of phenobarbitone or bromide withdrawal symptoms and lessening the toxic reactions incident to the commencement of administration of the new drug. It should be used with caution in debilitated patients or in the presence of cardiorenal disease.

In 142 patients with frequent convulsive seizures not relieved by other modes of therapy, the use of sodium diphenylhydantoinate in doses of from 0.2 to 0.6 g. a day over periods varying from 2 to 11 months, gave relief from "grand mal" attacks in 58% with greatly decreased frequency in a further 27%, and relief from "petit mal" attacks in 35% with greatly decreased frequency in a further 49%. There were no fatalities. A toxic dermatitis occurred in 10 patients, nonthrombocytopenic purpura in one patient and minor toxic reactions in 15%.—H. H. Merritt and T. J. Putnam, *J. Amer. med. Ass.*, ii/1938, 1068.

In the treatment of 75 cases mental improvement was observed in the majority. The importance of the toxic action of the drug is emphasised. Many cases exhibited toxic nervous symptoms, but only one developed a rash. These toxic symptoms often developed after an increase in the dose.—D. Blair *et al.*, *Lancet*, ii/1939, 363.

Results sufficiently favourable to warrant an extended trial, and in the younger and less deteriorated epileptics it seems that tolerance to the drug and the benefits therefrom are at least as good as with the other barbiturates. The drug provides in some cases the means of reducing for a time the total of seizures, and given in non-toxic doses it leads to amelioration in some cases where other drugs have not.—J. P. Steel and E. S. Smith, *Lancet*, ii/1939, 367.

Seems to be of value in the treatment of epilepsy in some cases, when other forms of treatment have failed, but there are no indications that it should supersede the less toxic anti-convulsants in the initial stages of treatment. Treatment of 91 chronic epileptics.—D. Williams, *Lancet*, ii/1939, 678.

Of use in the younger and better preserved patients, but on account of its toxic effects it is advisable not to maintain it for more than a few weeks at a time.—S. Davidson and J. D. Sutherland, *Brit. med. J.*, ii/1939, 720.

Will probably prove helpful in some cases of epilepsy, but it shows no promise of surpassing or even equalling phenobarbitone and it is a dangerous remedy, requiring particular circumspection in its use.—M. Critchley, *Practitioner*, ii/1939, 491.

Clinical observations on a group of 38 epileptic patients indicate that the drug possesses high therapeutic activity as an anticonvulsant. It has, however, marked side reactions, and should only be used if milder medication fails.—J. L. Fatterman, *J. Amer. med. Ass.*, i/1940, 396.

Out of 43 epileptics treated, 27 derived benefit in regard to both incidence of fits and psychological outlook. The margin between the therapeutic and the toxic dose is very small.—A. J. M. Butter, *Brit. med. J.*, i/1940, 483.

In the treatment of 60 epileptics the results were on the whole favourable and often striking in comparison with those obtained with other anticonvulsants. Improvement in general physical and mental condition and in the incidence of major and minor attacks. Mild toxic symptoms developed in 12 patients.—R. Coope and R. G. R. Burrows, *Lancet*, i/1940, 490.

**Phenylethylhydantoin.** (A foreign proprietary was formerly available under the Registered Trade Name NIVANOL).

[P1] "Phenylethylhydantoin; its salts; its acyl derivatives; their salts."

[S1] "Phenylethylhydantoin; its salts; its acyl derivatives; their salts."

[S7] *Medicines made up ready for the internal treatment of human ailments containing phenylethylhydantoin; its salts; its acyl derivatives; their salts, must be labelled with the words "Caution. It is dangerous to take this preparation except under medical supervision" instead of the word "Poison."*

*Dose.*—In chorea, the usual daily dose is 0.2 g. to 0.5 g. spread over 2 or 3 doses.

A tasteless crystalline powder, slightly soluble in water.

*Uses.* Hypnotic and sedative for use in the treatment of chorea. It must only be given under most careful supervision, and treatment must be stopped on the appearance of a rash or an increase in temperature. It should not be administered over lengthy periods.

In chorea, 0.3 g. *per os* daily for a child of 9 to 14 years. In most cases 8 to 14 days after beginning of treatment there is a well marked morbiliform rash accompanied by pyrexia. The drug is then stopped. It causes a change in the blood, *viz.*, a true eosinophilia reaching its maximum just before appearance of the rash. In addition there is generally a leucopenia. Conjunctivitis and oedema of the eyelids should be watched for and treatment stopped immediately. Report of 6 cases with beneficial results.—F. J. Poynton and B. Schlesinger, *Lancet*, ii/1929, 267.

Symptoms improved and attack sometimes cut short in a dramatic way. Only to be used under constant supervision.—C. F. T. East and E. R. Cullinan, *Lancet*, ii/1930, 190.

Purpura hæmorrhagica, nephritis, and a fatal case of dermatitis exfoliativa have followed its use in chorea. Effective, but catastrophe can neither be seen, foreseen nor prevented.—*Lancet*, ii/1931, 545.

No permanent benefit in three obstinate cases of chorea, and one patient suffered a dangerous reaction.—T. D. Jones and J. L. Jacobs, *J. Amer. med. Ass.*, ii/1932, 21.

Only used in severe and stubborn cases. The chief danger is temporary mental derangement and it is not advisable to give it to a mentally deficient child. The drug is stopped when the rash and large glands appear or if there is no reaction on the twelfth day. It is a drug that needs discretion but has been found very serviceable.—*Per Brit. med. J.*, i/1933, 903.

## BARIUM

Ba = 137.36.

[P1] "*Barium, salts of, other than barium sulphate and the salts of barium specified in Part II of this List.*"

[P2] "*Barium, salts of, the following:—Barium carbonate, barium silicofluoride.*"

[S1] "*Barium, salts of.*"

[S3] "*Barium, salts of—in witherite other than finely ground witherite.*"

[S6] "*Barium, salts of—specify proportion as the proportion of one particular barium salt which the preparation would be calculated to contain on the assumption that the barium (Ba) in the poison had been wholly converted into that salt.*"

Rule 10 of the Poisons Rules, 1935, exempts from the application of the Pharmacy and Poisons Act, 1933, and of the Rules made under that Act, all articles containing barium carbonate and prepared for the destruction of rats and mice.



[P1-S1] **Barii Chloridum.** *Syn.* BARIUM CHLORATUM (*P.G. VI*).  
 $\text{BaCl}_2 \cdot 2\text{H}_2\text{O} = 244.31$ .

*Dose.*— $\frac{1}{2}$  to 2 grains (0.03 to 0.12 g.). *P.G. VI* max. single dose 3 grains; or 9 grains *per diem*.

Colourless crystalline plates, with bitter saline taste. *Soluble* 1 in  $2\frac{1}{2}$  of water. Solution is destructive to bacteria. *Incompatible* with sulphates, phosphates, tartrates and carbonates.

*Antidotes.* Empty stomach by emetic or by stomach tube, using 2 oz. of magnesium sulphate in 2 gallons of water. Give 1-oz. doses of sodium or magnesium sulphate, well diluted, and repeated if necessary. Keep patient warm and give demulcent drinks. Stimulants for collapse.

*Uses.* It resembles digitalis in action and increases blood pressure by vasoconstriction, but is seldom used in therapeutics owing to its toxicity. It is used principally as a chemical reagent.

1% solution has been used as eye-wash in scrofulous inflammation.

Typhoid has been treated with barium chloride *per os* with good results in 33 out of 35 cases. *Dose.*—1 to  $1\frac{1}{2}$  grains, increased progressively to  $7\frac{1}{2}$  grains thrice daily for 6 to 7 days with intervals of 3 to 5 days.—*Prescriber*, 1929, 224. No bad results except vomiting. 1.5 g. each day in divided doses for 5 days, with 5-day interval, then repeated for further 5 days.—E. Petrina, *Brit. med. J. Epit.*, i/1931, 96.

**Barii Sulphas** (*B.P., Fr. Cx., P.G. VI, U.S.P. XI, etc.*).  
 $\text{BaSO}_4 = 233.4$ .

*Dose.*—For X-ray work only, 2 to 5 ounces (60 to 150 g. approx.) in a cornflour or other "meal" of about 6 to 15 ounces.

A white powder *insoluble* in water and acids.

For outlining portions of the alimentary tract, instead of bismuth carbonate and subnitrate (*q.v.*).

Barium sulphate suspensions in olive oil 10, 20%, etc., have been used for bladder examination.

[P1-S1] **Barium Thiosulphate** inadvertently administered in place of barium sulphate has caused death.

*Caution.*—*Barium carbonate* is also soluble and hence poisonous. Confusion with bismuth carbonate has occurred.

**Sulfate de Barium Gelatineux** (*Fr. Cx.*) is in paste form, containing 55 to 58% of water.

**Pulvis Barii Sulphatis Compositus** (*B.P.C.*). *Syn.* BARIUM MEAL, SHADOW MEAL.

Contains 75% of barium sulphate in a cocoa-flavoured powder.

*Dose.*—4 to 8 ounces (120 to 240 g.) mixed immediately before use with sufficient boiling water poured directly on to the powder.

**Emulsio Barii** (*Brompton H.*). Barium sulphate 4 oz., tragacanth 40 gr., water to 12 oz.

**Emulsio Barii Sulphatis** (*C.X.H.*). Barium sulphate 10 oz., essence of raspberry 60 m., soluble saccharin 1 gr., mucilage of tragacanth to 20 oz.

*Gt. Orm. H.* has barium sulphate 2 oz., dried milk 1 oz., sugar  $\frac{1}{2}$  oz., cocoa 40 gr., compound powder of tragacanth 30 gr.

*R.I. Edin.* has barium sulphate 1 oz., sugar half a teaspoonful, oatflour 2 teaspoonfuls, suspended in milk. This is given at 5 a.m. on the day of examination. At 10 a.m., shortly after the first series of radiographs has been taken, a second meal is given consisting of barium sulphate 4 oz., mucilage of acacia *q.s.*, water to 10 oz.

**St. Mark's H.** has barium sulphate 5 oz., tragacanth 45 gr., alcohol 90% 30 m., elixir of saccharin 30 m., vanillin  $\frac{1}{2}$  gr., water to 10 oz.

**U.C.H.** has barium sulphate 10 oz., mucilage of starch q.s., vanillin  $\frac{1}{2}$  gr., saccharin  $\frac{1}{2}$  gr., alcohol 90% 1 dr., chloroform 5 m., water to 1 pint. (For average dose.)

**Enema Barii Sulphatis (C.X.H.).** Barium sulphate 8 oz., mucilage of tragacanth to 20 oz. **U.C.H.** has barium sulphate 40 oz., tragacanth powder 1 dr., water to 80 oz.

**Barolac (Burroughs Wellcome, London).** A 30% suspension of finely divided barium sulphate containing no mucilaginous suspending agent.

**Fotamilko, Fotamealo and Fotonemal (Evans, Sons, Lescher & Webb, Liverpool).** Barium sulphate meals in powder form; the first contains dried full-cream milk and forms a thin, lemon-flavoured fluid; the second forms a thick cream containing tragacanth and flavoured with cocoa and sugar, and the third forms a simple, lemon-flavoured suspension.

**Nov-Umbrose (Allen & Hanburys, London).** Ready-mixed barium meal containing 75% of barium sulphate. Also supplied as a cream (a 1 in 1 preparation). **Umbrose** is a similar preparation.

**Shadoform (British Drug Houses, London).** Flavoured barium sulphate powder. **Shado-cream.** A 50% suspension ready for use.

[P1-81] **Baryta Sulphurata (B.P.C.).** *Syn.* BARIUM SULPHIDUM.  $BaS = 169.4$ .

**Dose.**— $\frac{1}{2}$  to 1 grain in pills coated so as to be more likely to dissolve in the intestines than in the stomach.

A greyish yellow powder, partially soluble in water, the solution decomposing slowly with loss of hydrogen sulphide. Has been given as an alternative in syphilitic affections, but its main use is as a depilatory.

[P1-81] **Barium Sulphide Depilatory.** *Syn.* CAUSTICUM BARIUM.

Barium sulphide, in fine powder from 1 to 3, wheat starch 3.

When required for use, make into a cream with water, spread on the part and let it remain five or ten minutes, then remove with a blunt knife. It temporarily reddens the skin.

[P1-81] *Another formula* is barium sulphide 5, powdered soap 1, French chalk 7, starch 7. One part of this mixed with 3 of water is applied and, to avoid possible dermatitis, is washed off after 5 minutes. May be used from time to time.

**Strontium Sulphide.**  $SrS = 119.7$ , is also used. A patented German preparation contained strontium sulphide 12, corn starch 40, talc 35, dextrin 7, nerolin 1, and essential oil 5 parts. It was claimed that the dextrin protects the skin and hair papilli and prevents the bad odour during use.

## BELLADONNA

*Syn.* DEADLY NIGHTSHADE.

[P1] "Alkaloids, the following; their salts, simple or complex:—*Belladonna, alkaloids of.*"

[81] "Alkaloids, the following; their salts, simple or complex:—*Belladonna, alkaloids of, except substances containing less than 0.15% of the alkaloids of belladonna calculated as hyoscyamine.*"

[86] "Alkaloids—*Belladonna, alkaloids of—specify proportion as the proportion of any one alkaloid of belladonna that the preparation would be calculated to contain on the assumption that all the alkaloids of belladonna in the preparation were that alkaloid.*"

*By Rule 10 of the Poisons Rules, 1935, machine-spread plasters are exempt from the provisions applying solely to substances in the First Schedule to the Rules.*

All parts of the plant *Atropa Belladonna* (Solanaceæ) yield the alkaloids hyoscyamine and atropine. The root contains from 0.3 to 0.8% of total alkaloids—chiefly hyoscyamine. Doubtful whether any atropine is present. Dried leaves of good quality contain 0.4 to 1%, principally hyoscyamine.

**Antidotes.** Treat as for poisoning by atropine, *see* p. 237.

[P1-S1] **Belladonnæ Folium** (B.P., U.S.P. XI, Fr. Cx., F.E. VIII, P. Belg. IV (as *Belladonnæ Pulvis*), and P. Helv. V) contains not less than 0.3% of total or mydriatic alkaloids calculated as hyoscyamine.

**Dose.**— $\frac{1}{2}$  to 3 grains (0.03 to 0.2 g.).

**Uses.** To check action of secretory glands. Powerful antispasmodic in intestinal colic, spasmodic asthma and bladder spasm due to calculi or prostatic irritation. Full doses of extract or tincture are useful in whooping cough and false croup, *e.g.*, 3 m. of the tincture for a child of one year, gradually increased to 10 m. Belladonna is often of value in enuresis; no rule can be fixed as to the quantity for any given age, but a child three or four years old may have 3 m. of the tincture in the afternoon and again in the evening before bedtime, and this may be increased gradually to 10 m. Broncho-pneumonia is sometimes well treated in the early stages by 4 to 5 m. doses of tincture or  $\frac{1}{4}$  gr. of extract every 3 or 4 hours, combined with diuretics and diaphoretics. In dyspepsia, belladonna reduces gastric secretion and inhibits spasmodic contractions. Large doses of tincture or extract are of value in post-encephalitic parkinsonism, *e.g.*, commencing with 7 m. of the tincture thrice daily for a week, increased to 10 m. for the second week, then to 15 m. and then to 20 m. (*see* also under *Belladonnæ Radix*).

[P1-S1] **Belladonna Pulverata** (B.P.). *Syn.* PULVIS BELLADONNÆ.

**Dose.**— $\frac{1}{2}$  to 3 gr. (0.03 to 0.2 g.).

Consists of belladonna leaf in fine powder adjusted with exhausted belladonna leaf to contain 0.3% of alkaloids calculated as hyoscyamine. It is officially required to be dispensed when *Belladonnæ Folium* is prescribed.

[P1] **Collyrium Belladonnæ** (B.P.C.). Green extract of belladonna 0.5% *w/v*.

[P1] **Collyrium Belladonnæ Compositum** (K.C.H.).

Boric acid 15 gr., quinine hydrochloride  $7\frac{1}{2}$  gr., liquid extract of belladonna 10 m., distilled water to 1 oz.

[P1-S1] **Emplastrum Belladonnæ Viride** (B.P.C.).

Contains dry extract of belladonna equivalent to 0.25% of alkaloids in rubber adhesive plaster. The machine-spread plaster is usually made with about four ounces of mass per square yard of bleached cotton cloth of plain weave. Perforations allow ventilation

and a covering of loosely attached muslin protects the adhesive surface.

[P1-S1] *Fr. Cx.* has belladonna extract (*Fr. Cx.*) 1, elemi 1, diachylon plaster (*Fr. Cx.*) 2.

[P1] **Emplastrum Belladonnæ et Capsici.**

A spread rubber-base plaster containing about 0.1% of belladonna alkaloids, and 0.25% of oleo-resin of capsicum.

[P1] **Emplastrum Belladonnæ, Capsici et Methylis Salicylatis.**

Similar to spread belladonna and capsicum plaster, but containing about 2% of methyl salicylate.

[P1-S1] **Extractum Belladonnæ Siccum (B.P.).** *Syn.* EXTRACTUM BELLADONNÆ ALCOHOLICUM.

*Dose.*— $\frac{1}{4}$  to 1 grain (0.016 to 0.06 g.).

This is prepared from the leaf—it is a mixture of alcoholic extract and powdered leaf, containing 1% of alkaloids. The more powdered leaf present in the extract the better it keeps. *P. Ital. V* is 1% total alkaloids made by means of 95% alcohol.

[P1-S1] **Extractum Belladonnæ (U.S.P. XI).**

*Average dose.*— $\frac{1}{4}$  grain (0.015 g.).

Two forms, pilular extract and powdered extract are official. They are of approximately the same strength as Extractum Belladonnæ *I.A.*

[P1-S1] **Extractum Belladonnæ (I.A.).** A "solid" extract (containing about 10% of water) prepared by means of alcohol 70% from the leaf, and containing 1.3% of the alkaloids of belladonna leaf.

[P1-S1] **Extractum Belladonnæ Viride (B.P.C.).**

*Dose.*— $\frac{1}{4}$  to 1 grain (0.016 to 0.06 g.).

A soft extract standardised to 1% w/v of alkaloids.

[P1-S1] **Glycerinum Belladonnæ (B.P.C.).**

Green extract of belladonna 50% w/w with boiling distilled water, and glycerin.

To check pain and inflammation, is often painted on boils, abscesses and carbuncles, and covered with a poultice; also applied on lint to the breasts to disperse milk.

[P1] **Linctus Belladonnæ (T.H.).** *Dose.*—1 drachm (4 ml.).

Tincture of belladonna 24 m., bismuth carbonate 24 gr., tincture of lemon 80 m., glycerin 80 m., water to 1 oz.

[P1] **Mist. Bellad. (N.I.F.).**

Potassium iodide 3 gr., liquid extract of ipecacuanha  $\frac{1}{2}$  m., tincture of belladonna 5 m., arsenical solution 2 m., chloroform water to  $\frac{1}{2}$  oz.

[P1] **Tinctura Belladonnæ (B.P., I.A.).**

*Dose.*—5 to 30 minims (0.3 to 2 ml.).

Prepared with about 10% of dried leaf, and standardised to contain 0.03% of alkaloids. *Fr. Cx.*, *P. Ital. V*, *P. Ned. V*, and *U.S.P. XI* are similar.

A fatal case of (most probably) chronic belladonna poisoning, in which 1 to 2 drachms of the tincture had been taken every day for 6 years.—J. Spears, *Brit. med. J.*, i/1927, 1105.

POST-ENCEPHALITIC PARKINSONISM well treated with tincture of belladonna, 45 minims daily.

A man who had been taking 1½ dr. of tincture of belladonna daily for many months with considerable benefit, began to lose ground. Suddenly he showed great improvement, which could not be accounted for until he admitted he had been taking double doses of his medicine. Many patients now take as large or larger doses without any toxic symptoms.—A. J. Hall, *Lancet*, i/1934, 595.

[P1-S1] **Bellafit** (*Richter, London*). Contains the total levorotatory alkaloids of the belladonna root. *Solution* for oral use contains 1 in 2000; *ampoules* contain 0.5 mg. in 1 ml.; *tablets* contain 0.25 mg. of total alkaloid. *Dose*.—1 or 2 tablets or 10 to 20 drops of solution three times daily, or 0.5 to 2 ml. daily by injection.

[P1-S1] **Bellafoline** (*Sandoz, London*). Preparations containing the natural alkaloids of belladonna leaf: *l*-hyoscyamine is present in an invariable and constant proportion with the secondary belladonna alkaloids (hyoscyne, atropamine and belladonine). *Tablets* contain  $\frac{2}{3}$  gr. total alkaloids; *solution* 1: 2000; 1 ml. ampoules =  $\frac{1}{16}$  gr.

[P1-S1-S4] **Belladrenal Tablets** (*Sandoz, London*). Contain  $\frac{2}{3}$  gr. of Bellafoline and  $\frac{1}{2}$  gr. of phenobarbitone. In angina pectoris, migraine and epilepsy.

[P1-S1-S4] **Bellergal Tablets** (*Sandoz, London*). Contain Bellafoline 0.0001 g., Femergin 0.0003 g., phenobarbitone 0.02 g. In diseases of the autonomic nervous system.

[P1] **Jocigares** (*Wilcox, Joseau, London*). Cigarettes containing extracts of belladonna, stramonium and digitalis. *Dose*.—4 to be smoked daily. For asthma and hay fever.

[P1-S1] **Belladonnae Radix** (*B.P., U.S.P. XI, P. Helv. V*).

*Dose*.— $\frac{1}{2}$  to 2 gr. (0.03 to 0.12 g.).

Contains not less than 0.4% of alkaloids calculated as hyoscyamine. *U.S.P. XI* and *P. Helv. V* require 0.45% of total alkaloids of belladonna.

**Uses.** Is used for the same purposes as the leaf, but chiefly in preparations for external use.

Relieves the pain of rheumatism, neuralgia, lumbago, chordee, and local inflammations, as of the breast. Also applied in phlebitis and to relieve the pain due to adhesions following pleurisy.

**The "Bulgarian Cure."** Good results are claimed to have been obtained in the treatment of post-encephalitic parkinsonism by the "Bulgarian Cure," an empirical method introduced by a Bulgarian apothecary, and consisting essentially of the administration of a decoction of Bulgarian belladonna root in white wine. The treatment had a considerable vogue on the Continent, especially in Italy, but clinical trials in this country have failed to show any specific therapeutic advantage in the use of Bulgarian root as compared with English root.

It has been established that Bulgarian belladonna root differs hardly at all from ordinary commercial root, except that its alkaloidal content seems to be considerably lower. The clinical trials, however, have indicated that administered in the form of a 5% extract, extremely large doses of belladonna alkaloids can be tolerated. The original decoction was prepared by boiling the root in white wine for fourteen minutes, filtering and cooling. Neuwahl and Fenwick (*Lancet*, ii/1937, 619), described the following method: 30 g. of root are macerated in 600 ml. of dry white wine containing 10 to 12% of alcohol for 5 to 6 hours. The resultant liquid is boiled for fourteen minutes, strained through cotton wool and stored in a refrigerator. The dosage recommended is initially 1 to 3 ml., increased daily by 1 to 3 ml. until an optimum dosage is achieved. Throughout the treatment the strictest clinical control is necessary.

#### **Alkaloidal Content.**

A sample of "Bulgarian" belladonna root differed hardly at all from ordinary

commercial root. Its alkaloidal content was lower, but tests seemed to indicate that the chemical constituents are the same.—A. E. Bailey, *Pharm. J.*, i/1938, 77.

In view of the potency and the large daily dosage of the decoction, it is important to realise the wide variation which may occur in the alkaloidal content of the drug. Reports so far received show that the limits may vary from 0.238 to 0.58% of alkaloids. The B.P. percolation process using 12% alcohol is a more suitable way of preparing a galenical than the hitherto described decoction processes, since it gives a more reliable preparation.—R. H. Henrikson, *Pharm. J.*, i/1938, 240.

The alkaloids of the Bulgarian root appear to be identical with those of other belladonna roots of commerce, and all these roots yield extracts with similar properties. It is suggested that simple maceration for 24 hours yields a preparation which represents the maximum amount of alkaloids available from the root. The white wine may be replaced by 1% acetic acid, with the addition of a small amount of alcohol or chloroform as preservative.—A. E. Bailey, *Pharm. J.*, i/1938, 567.

The pharmacognosy of the Bulgarian drug is essentially that of the official belladonna root, and its alkaloidal content is consistently lower. The nature of the alkaloids is probably the same. The following method of preparing an extract is recommended. Macerate 50 g. of drug in No. 60 powder for 24 hours in 1000 ml. of a menstruum consisting of lactic acid 2, syrup 5, alcohol 90% 16, water to 100. Strain and add 0.5% of chloroform.—S. A. Taylor and F. G. Hobart, *Pharm. J.*, ii/1938, 49.

#### Clinical Reports.

Excellent symptomatic results in post-encephalitic parkinsonism are claimed for the "Bulgarian treatment." It is stated to give better results than atropine and to be at the same time less toxic and very cheap. Description of two cases.—F. J. Neuwahl and C. C. Fenwick, *Lancet*, ii/1937, 619.

Clinical trials suggest that patients suffering from the parkinsonian syndrome can tolerate extremely large doses of belladonna alkaloids when administered in the form of a 5% extract in white wine or other menstruum. Such doses are well tolerated, and the dosage may safely reach and be maintained at an equivalent of 0.24 gr. of atropine.—A. E. Bailey, *Pharm. J.*, i/1938, 567.

14 patients suffering from post-encephalitic parkinsonism were treated with decoction of Bulgarian belladonna. Improvement was found in 10 patients. On substituting English belladonna the improvement in the parkinsonism was maintained, and the patients did not at first notice the substitution. There is no evidence that the therapeutic properties of Bulgarian belladonna differ from those of its English equivalent.—D. Hill, *Lancet*, ii/1938, 1048.

Treatment with an extract of Bulgarian belladonna was used in 123 cases of post-encephalitic parkinsonism over a period of 1½ years. The results were remarkably good in the majority of cases and no relapse was recorded. The original technique of preparing the decoction was discarded in favour of a method of cold extraction (method described). The activity of this preparation was found not to decline after a few weeks as did the wine decoction, and whereas the wine decoction varies in alkaloid content the content of the cold extraction is precisely known. Equally good results can be obtained, however, if English root is substituted for the Bulgarian. Toxic reactions result from the administration of high doses, and can be avoided by beginning with small doses gradually increased. The treatment is contraindicated and useless in cases of chronic encephalitis lethargica.—F. J. Neuwahl, *Lancet*, i/1939, 693.

As the result of a trial of the comparative effect of Bulgarian belladonna root, English belladonna root, and stramonium in five cases of post-encephalitic parkinsonism, it was concluded that there does not appear to be any advantage in using the Bulgarian belladonna in preference to the English, and that there was no appreciable difference between belladonna given as a decoction and belladonna given as the standard B.P. tincture.—N. S. Alcock and E. A. Carmichael, *Quart. J. Med.*, 1938, 565.

The claims that have been advanced in favour of the enhanced value of Bulgarian belladonna root in the therapeutic treatment of post-encephalitic conditions have not been confirmed.—*Rep. med. Offr. Minist. Hlth, Lond.*, 1938.

#### [P. 81] Chloroformum Belladonnæ (B.P.C.).

Contains the equivalent of 50% v/v of liquid extract of belladonna. Applied as a paint or on lint for neuralgia and rheumatism.

[P1-81] **Colloidum Belladonnæ (B.P.C.).** *Syn.* LIQUID BELLADONNA PLASTER.  
Liquid extract of belladonna 50% *v/v* and camphor 1.5% *w/v* in a colloidion basis. For application to joints, or where a plaster is unsuitable.

[P1-81] **Emplastrum Belladonnæ (B.P.).**

Contains 0.25% of the alkaloids of belladonna root, the aqueous-alcoholic percolate being evaporated and incorporated in plaster of colophony. Brown spread plasters usually consist of this colophony base plaster spread on bleached glazed calico of plain weave. Spread plasters prepared with a green mass in a rubber basis are also supplied and both forms are regarded as coming within the somewhat ambiguous official description.

Bee and wasp stings are well treated by belladonna plaster—if slight, left on short time; if severe (e.g., entered vein), several days may be necessary—gives considerable relief. Probably good for mosquito stings also.

Must not be applied by the midwife to mothers too ill to feed their babies, where there is heart disease, on account of paralysing effect of atropine on the vagus, with consequent quickening of heart's action.—W. H. F. Oxley, *Brit. med. J.*, 1/1931, 7.

[P1-81] **Emplastrum Belladonnæ (U.S.P. XI).**

A standardised spread plaster prepared with adhesive plaster and an extract of belladonna root.

[P1-81] **Extractum Belladonnæ Liquidum (B.P.).**

*Dose.*— $\frac{1}{4}$  to 1 minim (0.015 to 0.06 ml.).

Prepared from belladonna root by a percolation process, adjusting so that the extract contains 0.75% of alkaloids.

*P. Ital. V* contains 0.25% *w/v*.

[P1-81] **Fluidextractum Belladonnæ Radicis (U.S.P. XI).**

*Average dose.*— $\frac{1}{2}$  minim (0.05 ml.). Contains about 0.45% of alkaloids and is therefore about two-thirds the strength of the *B.P.* liquid extract.

[P1-81] **Linimentum Belladonnæ (B.P.).**

Prepared from belladonna root by percolation with a mixture of alcohol 90% (or I.M.S.) and water, and adjusted to contain 0.375% *w/v* of alkaloids, 5% *w/v* of camphor being added. A useful sedative for neuralgia and rheumatism.

Sprinkled on impermeable piline relieves lumbago.

[P1-81] **Linimentum Belladonnæ cum Chloroformo (B.P.C.).**

Chloroform, 1 in 8, with liniment of belladonna.

[P1] **Suppositorium Belladonnæ (B.P.).**

Contains  $2\frac{1}{2}$  m. (0.15 ml.) of liquid extract of belladonna in 1 g. of theobroma oil, i.e., 0.001 g. of root alkaloids.

[P1] **Pessaries** (60 grains weight) may also be made containing the same or double the quantity of extract.

Unilateral convulsions have been produced by their use, together with dryness of throat and dilated pupils (special idiosyncrasy).

[D-P1-81] **Suppositoria Belladonnæ**  $\frac{1}{2}$  grain, et **Morphinæ Hydrochloridi**  $\frac{1}{2}$  grain.

These possess a useful sedative effect, and are valuable in irritated and painful conditions of the rectum and prostate, and for chordee.

[P1-81] **Unguentum Belladonnæ (B.P.C.).**

Contains the equivalent of 80% *v/w* of liquid extract of belladonna, or 0.6% *w/w* of alkaloids, in a basis of wool fat and benzoinated lard.

Said to be too strong for general use and may cause unpleasant symptoms.

To lessen excessive secretion in nasal catarrh, this ointment has been employed diluted 5 to 10 times with soft petroleum and a small proportion of tannin or gallic acid added.

[P1·81] **Pommade Belladonnée** (*Fr. Cx.*). Extract of belladonna 10%, in glycerin and benzoated lard. It contains about 0·25% of belladonna alkaloids.

[P1] **Unguentum Belladonnæ** (*U.S.P. XI*).

Contains about 0·125% of belladonna alkaloids, and is prepared with 10 parts of pilular extract of belladonna rubbed down with 5 parts of diluted alcohol and incorporated with a melted mixture of wool fat 5, yellow wax 5, and petrolatum 75.

[P1] **Unguentum Populi** (*P. Belg. II*). Macerate dry belladonna leaves 125, dry henbane leaves 125 and dry poplar buds 200 (all bruised) in alcohol 90% 150 for 2 hours; warm on a water-bath with lard 1000 for 3 hours, stirring until the alcohol has evaporated. Strain, press and stir until the ointment sets.

**Zanthoxylum** (*B.P.C.*). *Syn.* XANTHOXYLUM, PRICKLY ASH BARK, TOOTHACHE BARK.

*Dose.*— $\frac{1}{2}$  to  $\frac{1}{4}$  drachm (1 to 2 g.).

The dried bark of *Z. americanum* or *Z. Clava-Herculis*. Carminative and gastro-intestinal stimulant producing diuresis and diaphoresis. A liquid extract has been used in the treatment of alcoholism.

## BENZENUM

*B.P.C., Fr. Cx.*

$C_6H_6 = 78\cdot11$ .

*Syn.* BENZOLUM (*P. Jap. V*).

*Dose.*—5 to 10 minims (0·3 to 0·6 ml.), in capsule or oily solution.

A colourless liquid obtained from light coal-tar oil. Sp. gr. 0·880 to 0·887. It solidifies at 0° and does not re-melt entirely below 4°.

Distinguish from **Petroleum Benzine** or **Benzoline**, the fraction of crude petroleum distilling below 150°. Light petroleum (petroleum ether) and petroleum benzine are used for heating cauteries for nævi, etc. Benzene is not suitable for this purpose—it burns with a smoky flame. It is, however, better for removing grease stains.

**Antidotes.** Empty stomach by emetic, or by stomach tube, using a suspension of 10 oz. of medicinal charcoal in 2 gallons of water. Keep patient in fresh air, apply artificial respiration and give oxygen, or oxygen with 7% carbon dioxide, inhalations. Stimulants, e.g.,  $\frac{1}{2}$  dr. of aromatic spirit of ammonia in water. Atropine,  $\frac{1}{100}$  gr., hypodermically. Nikethamide intravenously is said to be of value—5 to 10 ml. of 25% solution.

When swallowed it usually produces a sensation of burning in the stomach. It is a narcotic which, when swallowed or inhaled, produces vertigo, delirium and tonic convulsions, followed by deep sleep; 30 ml. has proved fatal.

Benzene poisoning, both acute and chronic, is an important



industrial hazard, especially in the rubber industry. The concentrated vapour is markedly toxic and may cause death. Workers suffering from chronic poisoning develop leucopenia, aplastic anæmia and purpura hæmolytica.

Nine cases of poisoning (with three deaths) in female workers employed in Belgian mirror factories to varnish mirrors which have been silvered; the second protective coat of varnish applied after silvering is a solution of gum-resins in benzol. The clinical picture is one of wasting, hæmorrhages and severe aplastic anæmia.—D. Gilbert, per *Brit. med. J.*, i/1937, 1157.

**Uses.** It quickly destroys pediculi capitis or pubis, applied freely; one application sufficient. For seborrhœa, should be brushed on the skin.

Leukæmia has been treated by large doses, e.g., 3 to 4 g. (45 to 60 minims approx.). Give small doses at first and note effects. It is advisable to discontinue the treatment as soon as the leucocytes start to decline, or at least when they have fallen to 20,000. The best results are obtained when the benzene is preceded by or continued with X-ray treatment.

The use of benzene is contraindicated in the presence of faulty functioning of the liver, kidneys, or intestines.

**Benzol** is a mixture of hydrocarbons obtained from light tar oil containing about 70% of benzene with toluene,  $C_6H_5-CH_3$ , and other hydrocarbons. Various grades are obtainable, e.g., 90% benzol, 50% benzol, etc., the figures indicating the proportion distilling below 100°.

**Cyclohexane.** *Syn.* HEXAMETHYLENE, HEXAHYDROBENZENE.  $C_6H_{12}$ . Is a colourless mobile liquid obtained by the hydrogenation of benzene. B.p. 81°. Is used as a solvent.

**Cyclohexanol.**  $C_6H_{11}OH$ . Is prepared by the catalytic hydrogenation of phenol, using nickel at about 180°. It is solvent for fats, waxes, resins, rubber, celluloid, etc., but is principally used in conjunction with soaps as a detergent, in laundry and textile work.

Its derivatives, cyclohexanyl acetate and cyclohexanone (SEXTONE, *Howards, Ilford*), and also methylcyclohexanol (SEXTOL; METHYLHEXALIN), produced by hydrogenation of the mixed cresols, and its acetate (SEXTATE), etc., are similarly employed.

**Benzoyl Chloride.**  $C_6H_5-COCl = 140.5$ . Prepared from phosphorus pentachloride and benzoic acid. Distils between 190° and 200°, sp. gr. 1.218. Distinguish from monochlorobenzene (*syn.* benzol chloride),  $C_6H_5Cl = 112.56$ , sp. gr. 1.106, b.p. 132°, and benzyl chloride,  $C_6H_5CH_2Cl = 126.5$ , sp. gr. 1.106, b.p. 178°; also benzal chloride (*syn.* benzylidene chloride or benzyl dichloride),  $C_6H_5CHCl_2 = 161.0$ , sp. gr. 1.288, b.p. 206°.

**Paradichlorbenzenum (B.P.C.).**  $C_6H_4Cl_2 = 147.0$ .

Colourless shining crystals with characteristic odour, m.p. 53° to 54°, slowly volatile in air. *Soluble* in benzene, ether and hot alcohol.

**Wood-Beetle Insecticide.** Paradichlorbenzene 92%, soap 3%, paraffin wax 3%, cedar wood oil 2%. Used in Westminster Hall.

Paradichlorbenzene when vaporised is effective for killing lice in clothing. Moles can be banished effectively by a teaspoonful placed in the runs at 6 to 8 feet intervals.

**Orthodichlorbenzene**, a heavy colourless liquid with characteristic odour, has also been used as wood and furniture preservative. A mixture of *o*-dichlorbenzene 9, soap 7, and oil of cedar wood 1 is effective against the death-watch beetle.

**Nitrobenzenum** (B.P.C.). *Syn.* NITROBENZOL, OIL OF MIRBANE.  
 $C_6H_5O_2N = 123.0$ .

[P2] "*Nitrobenzene.*"

[83] "*Nitrobenzene—in substances containing less than 0.1% of nitrobenzene; soaps containing less than 1% of nitrobenzene; polishes.*"

Pale yellow liquid with an odour similar to benzaldehyde. Used as an insect repellent and as preservative in polishes, etc. Largely used in chemical manufacture. Poisoning may occur from absorption through the skin or by inhalation of the vapour. It is a dangerous poison if used in sweetmeats.

**Antidotes.** Empty stomach by emetic or stomach tube. Give stimulants, but no alcohol or oils. Artificial respiration and oxygen with 7% carbon dioxide inhalations, if necessary. Strychnine  $\frac{1}{2}$  gr. hypodermically. Blood transfusion.

**Toluenum** (B.P.C.). *Syn.* TOLUOL, METHYLBENZENE.  
 $C_6H_5 \cdot CH_3 = 92.13$ .

A product of the distillation of coal tar, occurring as a colourless, mobile, highly inflammable liquid. B.p. about  $111^\circ$ , flash-point about  $7^\circ$ , sp. gr. about 0.87. Is used as a preservative of urine before chemical examination, and for sterilising catgut.

**Xylenum** (*Fr. Cx.*). *Syn.* XYLOL, XYLOLUM (*P. Helv. V*). A mixture of about 10% of *o*-, 70% of *m*-, and 20% of *p*-dimethylbenzenes,  $C_6H_4(CH_3)_2 = 106.1$ . B.p. about  $140^\circ$ . Has chemical and physical properties allied to benzene. The 1 : 2 xylene boils at  $141^\circ$ , 1 : 3 xylene boils at  $139^\circ$ , 1 : 4 xylene boils at  $138^\circ$ . Used as a microscopic cleaning agent and for sterilising catgut.

In dose of 5 to 15 minims in capsules, enteric-coated, has been employed in respiratory affections and in dyspepsia, and has also been suggested for use in certain skin diseases.

**Solvent Naphtha** consists of xylenes and trimethylbenzenes, b.p.  $140^\circ$  to  $180^\circ$ . Used as a solvent.

## BETANAPHTHOL

B.P., U.S.P. XI, *Fr. Cx.*, etc.

$C_{10}H_7OH = 144.2$ .

*Syn.* NAPHTHOL,  $\beta$ -HYDROXYNAPHTHALENE.

**Dose.**—5 to 10 grains (0.3 to 0.6 g.) in cachet. *Fr. Cx.* has max. single dose 15 grains, max. during 24 hours 45 grains approximately. U.S.P. XI average dose 4 grains.

Occurs in white or nearly white crystalline lamellæ or powder with a faint phenolic odour.

**Soluble** about 1 in 1000 of water, 1 in 2 of alcohol 90%, 3 in 4 of ether, 1 in 17 of chloroform, 1 in 24 of benzene, 1 in 12 of olive oil and lard, 1 in 80 of soft paraffin; also soluble in glycerin and in solutions of alkali hydroxides. Addition of boric acid increases solubility in water.

**Incompatible** with camphor, ferric chloride, menthol, phenazone and phenol.

**Uses.** Internally as intestinal antiseptic in enteric fever and putrefactive diarrhœa; safe and efficient, but sometimes causes too much gastric disturbance. In dilated stomach, dyspepsia and other

disorders. In cholera, as preventive, and in treatment of early stages. Is a vermifuge in ankylostomiasis; tablets containing betanaphthol 5 gr., and phenolphthalein 3 gr., are a useful combination for this purpose. It has also been found effective in ascariis infection and tapeworm. Large doses may cause toxic effects with symptoms of phenol poisoning. In kidney disease it is contraindicated.

It is a powerful antiseptic and germicide. In advanced scabies, an ointment of 10 to 15% cures the eczema as well as destroys the parasite, but the Compound Ointment is preferred. Useful also in psoriasis and other chronic skin diseases.

Betanaphthol 5, alcohol 100, glycerin 10, is a remedy for hyperhidrosis of palms, soles and axillæ.

TRACHOMA treated by "Oxidised Naphthol Camphor." The remedy should be freshly prepared, 2 parts of camphor and 1 of naphthol warmed gently and filtered, and the mixture allowed to oxidise in a clear glass vessel to syrup consistence and brown mahogany colour. The application is made with a small brush well soaked in the solution and then wiped nearly dry. Four to 10 applications suffice.

**Tabellæ Betanaphtholis (B.P.C.).** Contain 5 gr. (0.3 g.).

**Unguentum Betanaphtholis Compositum (B.P.C.).** *Syn.* KAPOSI'S COMPOUND OINTMENT, UNGUENTUM NAPHTHOL COMPOSITUM.

Betanaphthol about 1 in 11½, with chalk, in lard and soft soap. *L.H.* is practically identical.

**Unguentum Naphtholis (St. J.H.).** Betanaphthol 22 gr., sesame oil 6 dr., hard paraffin 30 gr., soft paraffin to 1 oz.

**Carbo Naphtholatus (P. Ital. V):** Betanaphthol 30, charcoal 40, magnesium oxide 30, mix, add alcohol 95% 50, and heat to form a coarse granular powder. Given in doses of 1 to 2 dr. in ailments of the stomach and intestines.

**Alphanaphthol (F.E. VIII).** *Syn.* α-HYDROXYNAPHTHALENE.

$C_{10}H_7 \cdot OH = 144.2$ .

*Dose.*—2 to 5 grains (0.12 to 0.3 g.). Larger doses are sometimes given.

In colourless crystals, m.p. about 94°. Is said to have greater antiseptic power, but given internally causes more irritation.

A solution of 1 in 3500 of water is used to wash out the intestines by rectal injection.

**Aluminii Naphtholsulphonas.** *Prop. Name.* ALUMNOL (*Bayer Products, London*). A whitish powder soluble 1 in 1½ of water, and in alcohol or glycerin. A mild antiseptic in ½ to 5% solutions. Used in solution or ointment, ½ to 2%, in rhinitis, ozæna and gonorrhœa.

**Napthithin (Wyleys, Coventry).** The lithium salt of β-hydroxynaphthalene-α-monosulphonic acid, a brownish-white odourless powder with a taste at first bitter, afterwards sweetish. Soluble in water (1 in 4), glycerin and alcohol. Incompatible with quinine salts. For gout, rheumatism, sciatica and lumbago.

*Dose.*—5 to 15 grains, maximum 60 grains per day.

**Betanaphthylis Benzoas (B.P.C., Fr. Cx., P. Ital. V, P. Belg. IV, P. Helv. V).** *Syn.* BENZONAPHTHOL, BENZOYL-NAPHTHOL, NAPHTHOL BENZOATE.  $C_{10}H_7 \cdot COOC_{10}H_7 = 248.3$ .

*Dose.*—5 to 15 grains (0.3 to 1 g.) in cachet or suspended.

A tasteless white crystalline powder. **Soluble** in alcohol, ether, and chloroform, almost insoluble in water. An intestinal antiseptic and diuretic, e.g., in typhoid. May be combined with bismuth salicylate. Externally is used 3 to 10% in ointments.

**Benzonaphthol Varnish.** Benzonaphthol 6, acetannin 10, salol 20, alcohol (90%) 30, ether 100, has been recommended as a varnish for pills to render them insoluble in the stomach, but no better results are obtained with it.

**Betanaphthylis Salicylas** (*B.P.C.*, *Fr. Cx.*). *Syn.* BETOL, NAPHTHALOL, NAPHTHOL SALICYLATE.  $C_8H_4(OH) \cdot COOC_{10}H_7 = 264.3$ .

*Dose.*—5 to 10 grains (0.3 to 0.6 g.) in cachets or pills, or suspended in mixtures or in almond emulsion or milk.

In small tasteless white crystals.

*Insoluble* in water, slightly soluble in cold alcohol 90%, soluble 1 in 3 of boiling alcohol, 1 in 15 of ether, and in benzene. Useful in rheumatism, cystitis, and intestinal catarrh.

**Naphthalenum** (*B.P.C.*, *P. Ned. V*, *P. Ital. V*, *P. Helv. V*).  $C_{10}H_8 = 128.1$ .

*Dose.*—3 to 12 grains (0.2 to 0.8 g.) in cachets.

2 g. administered in the course of two days has proved fatal to a six-year-old child.

A hydrocarbon formed in the manufacture of coal gas. In white crystalline plates (m.p.  $80^\circ$ ) with persistent odour.

*Soluble* 1 in 3 of ether, 1 in 23 of alcohol, 1 in 8 of olive oil, and 1 in  $1\frac{1}{2}$  of chloroform; insoluble in water.

*Antidotes.* Empty stomach by emetic or stomach tube. Give purgative dose of magnesium sulphate. Demulcent drinks, but *not* oils or fats.

The principal synthetic waxes are chloro-naphthalenes and chloro-diphenyls; they are made by passing chlorine through naphthalene or diphenyl. In the manufacture of monochlorodiphenyl, known as arachlor, and the chloro-naphthalenes, or halowax, the workers are liable to contract acne from exposure to fumes, and even symptoms of systemic poisoning, with digestive disturbances, hæmaturia, and finally death from yellow atrophy of the liver.—*L. Schwartz, Amer. J. publ. Hlth*, 1936, 26, 586.

*Uses.* As an intestinal disinfectant for the diarrhoea of consumption and of typhoid, and for dysentery, 8-grain enemata are useful. Internally, *e.g.*, in malt extract, with success to lessen fætor of urine and stools. A vermifuge in tænia and ascarides (for tapeworms a dose of 1 g. is given followed by castor oil). Suppository and ointment (10%) are used for pruritus ani. A 10 to 20% solution in oil is successful as a parasiticide in scabies.

N.C.I. Naphthalene of commerce 96, creosote 2, iodoform 2. Lice repellent.

**Naphthaleni Tetrachloridum** (*B.P.C.*). *Syn.* NAPHTHALIN HYDROCHLORIDE.  $C_{10}H_6Cl_4 = 289.9$ .

*Dose.*—3 to 12 grains (0.2 to 0.8 g.).

White crystals, m.p.  $185^\circ$  to  $187^\circ$ , insoluble in water.

Used for the same purposes as betanaphthol.

## BISMUTHUM

Bi = 209.0.

### Metallic Bismuth Preparations for Injection.

Bismuth metal has been largely used in conjunction with, and in some quarters instead of, the arsenicals in the treatment of

syphilis and yaws. The effectiveness of the antisyphilitic action of bismuth may be said to be intermediate between arsphenamine and mercury. The preparations used are summarised.

**Bismuthum Præcipitatum (B.P.).**

*Dose.*— $1\frac{1}{2}$  to 3 grains (0.1 to 0.2 g.) by intramuscular injection.

Prepared by the reduction of bismuth trichloride in hydrochloric acid solution by means of hypophosphorous acid. A dull grey powder containing no particles greater than 15 microns in diameter.

**Injectio Bismuthi (B.P.).** *Prop. Names.* BISGLUCOL (*Pharmaceutical Specialities (May & Baker) Ltd., London*), BISMOSTAB (*Boots, Nottingham*).

*Dose.*—8 to 15 minims (0.5 to 1 ml.).

Contains 20% w/v of precipitated bismuth with 0.5% v/v of cresol in isotonic dextrose solution.

For bismuth injections an all-glass syringe should be used, since nickel poisoning has been known to occur from the use of a syringe with a nickel-plated piston.

Bismuth injections are given intramuscularly. Intravenous injections are too dangerous, and hypodermic injections too irritant.

**Toxic Effects.** With intramuscular injections serious toxic effects are rare if administration is stopped at the first warning symptoms, namely, foul breath, blue line on the gums and mild stomatitis. If these warnings are ignored, however, serious ulcerative stomatitis may result, together with other toxic effects such as nausea, loss of appetite, headache, depression, diarrhoea, albuminuria, skin reactions, possibly exfoliative dermatitis, and even jaundice. The mouth, digestion, skin and urine should be watched and oral hygiene insisted on. Septic conditions of the mouth are contraindications.

Severe stomatitis from injection of metallic bismuth may be treated by intravenous injections of 5 ml. of 10% sodium thiosulphate solution on alternate days.

**BISMUTH JAUNDICE.** Although jaundice from bismuth injections has been largely unrecognised it does occur. The incidence of bismuth jaundice over a period of 5 years at one clinic has been one attack for 2242 injections of bismuth compounds (the incidence of jaundice from nearsphenamine during the same period being one attack for each 951 injections). A report of 32 cases of bismuth jaundice.—R. Nomland, *J. Amer. med. Ass.*, ii/1938, 19.

*For details of a suggested course of combined treatment of syphilis with arsenic and mercury or bismuth, see under Arsphenamina, p. 231.*

**Bicreol (Burroughs Wellcome, London).** *Dose.*—1 to 2 millilitres intramuscularly, alternating with nearsphenamine injections. Contains bismuth metal 0.15 g. per ml. in a Creol-Camph base.

**Bismoid (Lilly, London).** Bismuth metal suspension in an aqueous medium containing approximately 5% of carbohydrate and dextrose derivatives (1 ml. = 0.025 g. of bismuth).

**Bi-Liposol (Modern Pharmaceuticals, London).** Oily solution of camphor carbonate of bismuth (1 ml. = 4 ctg. Bi). *Dose.*—2 ml. intramuscularly twice a week. In syphilis and yaws.

**Biscam** (*Modern Pharmaceuticals, London*). A suspension of bismuth camphorate in olive oil. *Dose*.—2 ml. intramuscularly every 3, 5, or 7 days for 12 to 18 injections. In syphilis and yaws.

**Bivatol** (*Laboratoire Français de Chimiothérapie, Paris; Anglo-French Drug Co., London*). Basic bismuth  $\alpha$ -carboxethyl- $\beta$ -methylnonoate. A lipo-soluble bismuth compound supplied in ampoules containing 2 ml. (=0.07 g. of bismuth), for intramuscular injection in syphilis. (*This preparation is marketed in U.S.A. under the name Biliposol.*)

**Neo-cardyl** (*Pharmaceutical Specialities (May & Baker) Ltd., London*). Bismuth butylthiolaurate in oily solution (1 ml. = 0.05 g. Bi). *Dose*.—1.5 ml. intramuscularly at 5-day intervals for 12 doses. Syphilis.

**Stabismol** (*Boots, Nottingham*). Basic bismuth  $\alpha$ -carbethoxy-cyclo-hexanyl acetate. 10% bismuth in olive oil. *Dose*.—When given alone, from 1 to 2 ml. weekly intramuscularly in doses of 0.5 to 1 ml. at intervals of 2 or 3 days, for from 4 to 8 weeks. Also given concurrently with the arsenamines.

### Bismuth Salts and Compounds.

The absorbent action of the preparations of bismuth taken internally is increased by combination with antiseptic compounds. These combinations have been much recommended in those disorders of the digestive tract in which several infectious diseases make their early manifestation. Thus the salicylate, and naphthol, phenol, pyrogallol and bromophenol compounds have been brought into use. These check the fermentative processes forming ptomaines, yet, it is said, do not interfere with intestinal digestion.

Owing to the limited gastro-intestinal absorption, oral administration of bismuth does not give rise to toxic effects, except that large doses of the subnitrate may cause nitrite poisoning.

Bismuth compounds are in general *incompatible* with potassium iodide, the insoluble brown bismuth tri-iodide being formed.

**Bismuthi Benzoas.** *Syn.* BISMUTH OXYBENZOATE.  $C_6H_5 \cdot COO(BiO) = 346.0$ . *Dose*.—5 to 20 grains (0.3 to 1.2 g.) thrice daily.

A white powder insoluble in water, containing the equivalent of about 65% of  $Bi_2O_3$ . Antiseptic, internally in gastro-intestinal diseases, externally to chancre, indolent and sloughing ulcers.

**Benzo-Bismuth** (*Anglo-French Drug Co., London*). Sodium salt of trioxo-bismuthobenzoic acid. Ampoules contain 0.2 g. (0.04 g. of Bi). *Dose*.—1 ampoule intramuscularly twice weekly for 7 to 8 weeks, allowing a rest of 3 to 6 weeks between each series of 15 injections. In syphilis.

**Neo-Olesal** (*Bayer Products, London*). 10% solution of bismuth dimethyl-endomethylene-hexahydrobenzoate in oil. *Dose*.—2 ml. intramuscularly 2 or 3 times weekly up to a total dosage of 25 or 30 ml. In all stages of syphilis.

**Bismuthi Carbonas** (*B.P., U.S.P. XI, Fr. Cx., P. Helv. V, etc.*). *Syn.* BISMUTH OXYCARBONATE OR SUBCARBONATE. Composition varies slightly, but it approximates to  $(Bi_2O_2CO_3)_2 \cdot H_2O = 1038.1$ .

*Dose*.—10 to 30 grains (0.6 to 2 g.).

A white, odourless, tasteless powder, stable in air. The light varieties need no suspending agent.

*Insoluble* in water and organic solvents; soluble in acids with effervescence.

*Uses*.—Internally in dyspepsia, gastric inflammation and diarrhoea, forming a protective coating on the walls of the stomach and intestines; also with alkalis in the treatment of gastric and duodenal ulcer. Is also stated to be effective in the treatment of ascaris and

thread-worms. Externally, is sedative and astringent, in ointments and dusting powders. Has been used as a contrast medium in X-ray work.

**DYSENTERY.** Bismuth subcarbonate is a most useful adjunct in acute dysenteric cases. Subnitrate of bismuth is not used because of possible untoward nitrite effects, such as methæmoglobinæmia and methæmoglobinuria, following the administration of excessive amounts of the drug in susceptible individuals.—H. A. Anderson, *J. trop. Med. (Hyg.)*, 1935, 271.

**THREAD-WORMS.** Bismuth carbonate, as suggested by Loeper, a specific. For an adult 3 doses of 20 gr. at intervals of 4 hours, and for a child under 7 years 10 to 40 gr. per dose. Simple and instantaneous cure.—G. Simpson, *Brit. med. J.*, ii/1929, 604. Correspondence on treatment.—*Brit. med. J.*, ii/1931, 517.

**X-RAY DIAGNOSIS.** Bronchoscopic insufflation with bismuth carbonate of value in radiography of the lungs. One ounce can be safely used in adults.

**Enema Bismuthi (B.P.C.).** Dose.—20 ounces (600 ml.). Bismuth carbonate or subchloride 30% w/v in mucilage of starch.

**Glycerinum Bismuthi Carbonatis (B.P.C.).**

Dose.—10 to 60 minims (0.6 to 4 ml.).

Bismuth carbonate 50% w/v, in distilled water and glycerin.

**Mist. Bismuth. (N.I.F.).** Syn. MIST. BISMUTH. C. SODA.

Bismuth carbonate 5 gr., sodium bicarbonate 10 gr., light magnesium carbonate 10 gr., peppermint water to  $\frac{1}{2}$  oz.

**Mistura Bismuthi cum Catechu (P.E.H.C.).** For 1 year old child.

Bismuth carbonate 5 gr., sodium bicarbonate 2 gr., tincture of catechu 3 m., compound tincture of cardamom 5 m., spirit of chloroform 1 m., glycerin 15 m., water to 1 dr.

[P1] **Mistura Bismuthi et Pancreatini (B.P.C.).**

Dose.— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.).

Bismuth carbonate 10 gr., sodium bicarbonate 10 gr., pancreatin 4 gr., dilute hydrocyanic acid 2 m., in chloroform water to 1 oz.

**Mistura Bismuthi et Sodii Bicarbonatis (B.P.C.).**

Syn. MISTURA BISMUTHI CUM SODA.

Dose.— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.).

Contains 10 grains each of bismuth carbonate, sodium bicarbonate and light magnesium carbonate in 1 oz.

**Mist. Bismuth. Fort. (N.I.F.).**

Bismuth carbonate 10 gr., sodium bicarbonate 10 gr., heavy magnesium carbonate 10 gr., peppermint water to  $\frac{1}{2}$  oz.

[P1] **Mist. Bismuth. Sed. (N.I.F.).**

Bismuth carbonate 5 gr., sodium bicarbonate 10 gr., chalk 5 gr., tincture of chloroform and morphine 10 m., water to  $\frac{1}{2}$  oz.

[P1] **Mist. Bismuth. Sed. Fort. (N.I.F.).**

Bismuth carbonate 10 gr., sodium bicarbonate 10 gr., solution of morphine hydrochloride 5 m., chloroform water to  $\frac{1}{2}$  oz.

**Pasta Bismuthi (B.P.C.).**

Bismuth carbonate 30% in white soft paraffin.

**Pulvis Bismuthi Compositus (B.P.C.).** Caution.—This name was formerly applied to Ferrier's snuff.

Dose.— $\frac{1}{2}$  to 1 drachm (1 to 4 g.).

Bismuth carbonate 1, calcium carbonate 3, heavy magnesium carbonate 3, sodium bicarbonate 1.

For the treatment of gastric and duodenal ulcer. This is usually

supplied for MacLean's powder. *N.I.F.* has the same proportions but specifies chalk instead of the purer calcium carbonate, thus agreeing with MacLean's original Formula II (for hospital use). Formula I contained bismuth carbonate 2, sodium bicarbonate 1, heavy magnesium carbonate 2. Administration of alkaline powders must be accompanied by dietary control, as in the following scheme (H. MacLean and co-workers, *Lancet*, i/1928, 14; *Brit. med. J.*, i/1928, 619):

*First Week.* A teaspoonful in a little water or milk 6 or 7 times daily (preceded by a glass of milk with 10 grains sodium citrate added to prevent coagulation), with double dose last thing at night and extra powder during night if patient wakes. If bowels disturbed excessively, adjust powder or add magnesia cream.  
*Second Week.* If discomfort and symptoms still persist continue as first week for a few days, otherwise reduce powder to 4 or 5 doses daily and reduce milk, adding beaten up eggs and gradually increasing diet so that by end of week patient is receiving toast, butter, eggs, custard, and cream. Dose immediately before retiring and during night as before.  
*Third Week.* Reduce to 3 or 4 doses daily and one at bedtime and increase food to include fish and potatoes and cereal puddings.  
*4th to 6th Weeks.* Powder 3 times daily, with dose at bedtime and reduce or give up milk. A small amount of meat may be taken the 5th week.  
*After-treatment.* Continue powder two or three times daily for further 6 weeks, with a dose at bedtime for a long time afterwards, and return to milk or light diet with powder 4 or 5 times daily if symptoms return at any time. Smoking and alcohol should be avoided.

Two cases in which the regular taking of an alkaline mixture, associated with an ulcer dietetic régime, was responsible for the formation of primary phosphatic renal stones. The most important part of the medical treatment of peptic ulcer must always be somewhat small and oft-repeated meals. This fact is unfortunately little recognised by medical practitioners, who regard the alkaline mixture as the *sine qua non* of ulcer treatment. The profession should be warned of the intimate relation of the formation of calculi to the consumption of large doses of alkaline powders.—T. Moore, *Lancet*, ii/1939, 1118.

**Tabellæ Bismuthi Carbonatis (B.P.C.)** contain 5 gr. (0.3 g.).

**Tabellæ Bismuthi et Sodii Bicarbonatis (B.P.C.).** Dose.—1 to 3 tablets. Contain 2 gr. of bismuth carbonate and 3 gr. of sodium bicarbonate.

**Trochisci Alkalini Compositi (B.P.C.).** Each lozenge contains 12 gr. of compound bismuth powder.

**Trochiscus Bismuthi Compositus (B.P.).** Contains  $2\frac{1}{2}$  gr. each of bismuth carbonate and heavy magnesium carbonate and  $4\frac{1}{2}$  gr. of calcium carbonate.

**Unguentum Bismuthi (B.P.C.).**

Bismuth carbonate 12½% in white soft paraffin.

[P2] **Ung. Bismuth. c. Camph. (N.I.F.).** For hæmorrhoids.

Liquefied phenol 20 m., camphor 4 gr., bismuth carbonate 120 gr., ointment of zinc oxide 240 gr., white soft paraffin to 480 gr.

[D-P1-81] **Unguentum Bismuthi Morphine et Cocaine (Allingham).** Bismuth carbonate 20, morphine hydrochloride  $\frac{1}{2}$ , cocaine hydrochloride 3, soft paraffin to 100. Useful as astringent in hæmorrhoids and for allaying irritation.

**Antacid Lozenges (Parke, Davis, London).** Takadiastase, bismuth carbonate, magnesium carbonate, oleoresin of ginger and oil of peppermint. Dose.—1 to 3 lozenges. To neutralise gastric acidity.

**Crema-Carbonates (Sharp & Dohme, London).** Each fluid ounce contains bismuth carbonate 20 gr., magnesium carbonate 20 gr., calcium carbonate 10 gr., chloroform 1 m.

**Sanusin Sempules (British Drug Houses, London).** Suppositories containing resorcinol, boric acid, balsam of peru, zinc and bismuth carbonate. Useful in treatment of hæmorrhoids.

**Bismuthi Citras (B.P.C.).**

Dose.—2 to 5 grains (0.12 to 0.3 g.).

A white crystalline powder, yielding from 55 to 59% of  $\text{Bi}_2\text{O}_3$ .



It is probably a monobismuthylcitric acid,  $\text{H}_2\text{C}_6\text{H}_5\text{O}_7(\text{BiO})$ . Insoluble in water and alcohol 90%, but soluble in ammonia. It is astringent and stomachic.

**Bismuth Citrate Gauze.** May replace iodoform gauze, being non-toxic and without odour. May be left in uterine cavity at least five days and still be free from offensiveness. For use after curettings, in nasal and aural surgery and for burns.

**Bismuthi et Ammonii Citras (B.P.C.).**

*Dose.*—2 to 5 grains (0.12 to 0.3 g.).

In soluble shining pearly or translucent scales containing 46 to 50% of  $\text{Bi}_2\text{O}_3$ .

**Liquor Bismuthi Concentratus (B.P.C.).**

*Dose.*— $\frac{1}{4}$  to  $\frac{1}{2}$  drachm (1 to 2 ml.).

Is twice the strength of Liquor Bismuthi et Ammonii Citratis, containing the equivalent of 10 to 12% w/v of  $\text{Bi}_2\text{O}_3$ .

**Liquor Bismuthi et Ammonii Citratis (B.P.C.).**

*Syn.* LIQUOR BISMUTHI, LIQUOR BISMUTHI CITRATIS.

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Contains the equivalent of 5 to 6% w/v of  $\text{Bi}_2\text{O}_3$ . May be prepared by dissolving bismuth citrate 10% w/v in solution of ammonia and diluting to volume, filtering if necessary.

If prepared with the minimum amount of ammonia (as in B.P.C.) the solution will give a precipitate when dispensed with sodium bicarbonate; if slightly alkaline no precipitate is produced.

When prescribed with glycerin of phenol, the mixture quickly develops a blue coloration if exposed to light.—*Pharm. J.*, ii/1933, 73.

**[P1] Mistura Bismuthi Composita (B.P.C.).**

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

1 dr. contains  $\frac{1}{2}$  dr. of concentrated solution of bismuth,  $7\frac{1}{2}$  m. of tincture of nux vomica, and 2 m. of dilute hydrocyanic acid.

Is also available with pepsin 1 gr. per drachm (**Mistura Bismuthi Composita cum Pepsino B.P.C.**) and with 1 gr. of pepsin and  $\frac{1}{16}$  gr. of morphine hydrochloride per drachm (**Mistura Bismuthi Composita cum Pepsino et Morphina B.P.C.**).

**Mist. Bismuth. et Ammon. Cit. (N.I.F.).** Solution of bismuth and ammonium citrate 40 m., strong solution of ammonium citrate 4 m., sodium bicarbonate 10 gr., solution of bordeaux B  $2\frac{1}{2}$  m., chloroform water to  $\frac{1}{2}$  oz.

**[P1] Bisedia (Giles, Schacht, Bristol).** *Dose.*—1 drachm (4 ml.) containing bismuth and pepsin with  $\frac{1}{16}$  gr. of morphine hydrochloride, 2 m. of hydrocyanic acid, and 5 m. of tincture of nux vomica.

**Bismuthi et Cinchonidinæ Iodidum.**  $\text{C}_{12}\text{H}_{22}\text{N}_2\text{O} \cdot \text{HI} + \text{BiI}_3 = 1011.9$ .

*Dose.*— $\frac{1}{4}$  to 1 grain (0.01 to 0.06 g.).

Yellowish-red powder insoluble in ordinary solvents, containing about 20% bismuth, 40% each iodine and cinchonidine.

**Bismuthi et Sodii Tartras (B.P.C.).**

*Syn.* SOLUBLE BISMUTH TARTRATE, ACID BISMUTH SODIUM TARTRATE.

**Caution.** This is the acid compound; to be distinguished from Bismuthi et Sodii Tartras (B.P. Add. I) which is a neutral bismuthyltartrate. The acid compound is not suitable for injection.

*Dose.*—2 to 5 grains (0.12 to 0.3 g.) *per os*.

Colourless scales with acid reaction containing 38 to 44% of Bi.  
**Soluble** in water.

**Uses.** For digestive complaints, in conjunction with pepsin, the acid solution favouring the action of the enzyme with which it is compatible in moderate amount.

**Liquor Bismuthi Acidus (B.P.C.).**

**Dose.**— $\frac{1}{2}$  to  $\frac{1}{2}$  drachm (1 to 2 ml.).

A solution of acid bismuth sodium tartrate, containing the equivalent of 9 to 10% w/v of  $\text{Bi}_2\text{O}_3$ .

[P1] **Mistura Bismuthi Composita Acida cum Pepsino (B.P.C.).**

**Dose.**— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

One drachm contains acid solution of bismuth equivalent to about 5 gr. of bismuth sodium tartrate, 1 gr. of pepsin, and  $\frac{1}{2}$  m. of liquid extract of nuxvomica.

The acidity of the mixture maintains the activity of the pepsin.

**Mist. Bismuth. c. Pepsin. (N.I.F.).** Compound acid mixture of bismuth with pepsin 30 m., water to  $\frac{1}{2}$  oz.

**Bismuthi et Sodii Tartras (B.P. Add. I).**

**Syn. and Prop. Name.** BISMUTH SODIUM TARTRATE, SODIUM BISMUTHYL TARTRATE, SODIUM TARTROBISMUTHATE, SOBITA (*Howards, Ilford*).

**Caution.** This is the neutral compound; to be distinguished from Bismuthi et Sodii Tartras (B.P.C.) which is an acid bismuthyltartrate.

**Dose.**—1 to 3 grains (0.06 to 0.2 g.) by intramuscular injection.

A white powder or yellowish scales containing 35 to 42% of Bi.

**Soluble** 1 in less than 1 of water.

**Uses.** Is administered intramuscularly in the treatment of syphilis. May be dissolved in water, saline or dextrose solutions, or suspended in oil. Oily suspensions are commonly preferred because less painful, and more slowly absorbed, hence less likely to cause toxic symptoms. Employed as a 1.5% solution, or stronger in suspension. The injections exert a marked diuretic action.

**DIURESIS.** In doses of 0.03 g. intramuscularly bismuth sodium tartrate has a powerful diuretic action, more effective than Novasurol and with no ill effects except occasionally a local abscess at site of injection.—Clifford Hoyle, *Practitioner*, ii/1933, 428. See also P. J. Hanzlik and co-workers, *J. Amer. med. Ass.*, i/1929, 1416.

**SYPHILIS, AORTIC.** Pain, the most common symptom in 100 cases of aortic syphilis, was relieved in all but one case by sodium bismuth tartrate intramuscularly in doses of 2 ml. of a 1.5% solution twice a week in courses of 10 injections.—L. M. Blackford and J. H. Boland, *J. Amer. med. Ass.*, ii/1932, 1902.

**Bismuthi et Potassii Tartras (U.S.P.XI).** **Syn.** POTASSIUM BISMUTH TARTRATE, POTASSIUM BISMUTHYL TARTRATE.

**Average dose.**— $2\frac{1}{2}$  grains (0.15 g.) by injection.

A white powder **soluble** 1 in 2 of water. Contains the equivalent of 71 to 75% of  $\text{Bi}_2\text{O}_3$  (about 64 to 67% of Bi). Given intramuscularly in syphilis in solution or suspension, as the sodium

compound. It is stated to disappear completely from the site of injection, usually in 2 weeks.

**Potassium Bismuthyl Saccharate** has been prepared by the addition of freshly precipitated bismuth hydroxide to a solution of potassium acid saccharate. It was obtained as a white solid, soluble in water, but insoluble in organic solvents.

It has been shown to be a more stable complex than the corresponding tartrate and gluconate, and since its solution appears to be stable indefinitely, it is of interest as a drug for the treatment of those diseases for which bismuth is used.—G. O. Doak, *J. Amer. pharm. Ass., Sci. Edn.*, 1940, 108.

Injected intramuscularly it is gradually absorbed and excreted. Bismuth is present in all the organs and tissue fluids within 24 hours, resulting in fairly uniform blood bismuth levels for five days.—C. W. Sondern *et al.*, *J. Amer. pharm. Ass., Sci. Edn.*, 1940, 346.

**Sodium Potassium Bismuthyltartrate.** *Syn.* SODIUM POTASSIUM TARTROBISMUTHATE.

**Dose.**— $1\frac{1}{2}$  to 3 grains (0.1 to 0.2 g.) intramuscularly, in solution in saline, or in suspension in 1 to 2 ml. of vegetable oil. Is injected once or twice weekly until 30 to 45 gr. has been given.

A white powder *soluble* about 1 in 2 parts of water, giving a neutral solution.

Used in syphilis and yaws, but the difference in effect between it and a body without the potassium compound is no doubt negligible.

**RELAPSING FEVER.** Sodium potassium bismuth tartrate brings fever down. Given intramuscularly—for an adult, 2 injections of 0.2 g. in 2 ml. water, for a child of 2 to 10 years 2 injections each of 0.1 g. For a baby under 2 years, 1 injection of 0.1 g.—J. Todd, *Brit. med. J.*, i/1930, 312.

**Sodium Bismuthate.** A yellow-brown, hygroscopic powder containing about 85% of  $\text{NaBiO}_3$ , with bismuth oxide and water. It slowly decomposes on keeping.

*Insoluble* in water. Boiled with water it decomposes into bismuth oxide and sodium hydroxide, and liberates oxygen.

Medicinally it is used in the preparation of sobisminol mass (*q.v.*).

**Sobisminol Mass.**

**Dose.**—25 to 34 grains (1.5 to 2.25 g.) thrice daily.

It is supplied in capsules, each containing 0.75 g., equivalent to 150 mg. of Bi.

Sobisminol mass is a complex substance obtained by the interaction of sodium bismuthate, triisopropanolamine and propylene glycol. It contains about 20% of Bi, and occurs as a chocolate-coloured pasty mass with a bitter taste.

During 1933 P. J. Hanzlik undertook to develop a soluble bismuth preparation intended for oral as well as intramuscular administration in the treatment of syphilis. A patent was applied for by Hanzlik in 1936, and later three manufacturers (E. R. Squibb & Sons; Cutter Laboratories; and Eli Lilly & Co.) were licensed by the Board of Trustees of Stanford University of California to manufacture the preparation, the word "Sobisminol" being decided on as a suitable non-proprietary designation by Hanzlik, the manufacturers and the Council on Pharmacy and Chemistry of the A.M.A.—*J. Amer. med. Ass.*, ii/1939, 2235.

*Soluble* in water and alcohol, but less soluble in ether and acetone. The pH of a 10% w/v aqueous solution should not be above 11.9.

**Uses.** For use in the treatment of syphilis by the oral route. It is particularly indicated for those patients unable to undergo intramuscular bismuth therapy, and to supplant therapy by that route for patients compelled for a time to be out of contact with their physicians. It may also be indicated in congenital and latent syphilis. It should be employed only under medical supervision. The patient should be watched for evidence of gastro-intestinal upsets and bismuth intoxication.

The adult dosage is from 2 to 3 capsules three times a day, taken with plenty of water at 10 a.m., 3 p.m. and 8 p.m. Unless contraindications arise this therapy may be continued for 10 to 12 weeks, and represents a course of bismuth therapy. For children the dosage may be cut down to one capsule three times a day or a 75 mg. capsule three times a day for a very young child.

Daily doses of 6 capsules by the mouth brings about involution of active syphilitic lesions of the skin in periods comparing favourably with those when preparations for intramuscular administration are used. The time required in cases of primary and secondary syphilis is only slightly greater than when neoarsphenamine is used. A similar dosage brings relief from the symptoms of late neuro-syphilis (particularly tabetic) in a high percentage of cases, and appears to offer a definite advantage over any other drug hitherto used. It is well tolerated by most patients and can be used daily for many months without cumulative toxic effects.—J. R. Scholtz *et al.*, *J. Amer. med. Ass.*, ii/1939, 2219.

A valuable addition to anti-syphilitic therapy deserving of further clinical trial.—W. M. Meininger and C. W. Barnet, *ibid.*, 2214.

### **Sobisminol Solution.**

**Dose.**—15 to 30 minims (1 to 2 ml.) by intramuscular injection twice weekly.

It consists of a solution of sobisminol mass in a mixture of propylene glycol and water. 1 ml. contains about 20 mg. of bismuth and 0.5 ml. of propylene glycol. Sobisminol solution is dark red in colour and is miscible with an equal volume of water or alcohol. pH 11.1 to 11.5.

**Uses.** Sobisminol solution is proposed for use in all types of syphilis, and is claimed to be free from unusual discomfort (see *J. Amer. med. Ass.*, ii/1939, 2238). It is given intramuscularly in a dose of 1 to 2 ml. twice a week for a series of 20 to 25 injections. In cases of arsenical sensitisation the injections may be continued for a much longer period.

**Sobisminol** (*Lilly, London*). A solution containing sodium bismuthate 3% in a mixture of triiso-propanolamine 8%, propylene glycol 50%, and water, a 1 ml. dose containing approximately 20 mg. of Bi. Capsules (**Sobisminol Mass**) containing 150 mg. of Bi in 0.75 g. are also available for oral administration.

[P1-81] **Bismuthi Arsanilas.**  $\text{BiO} \cdot \text{O} \cdot \text{AsO}(\text{OH}) \cdot \text{C}_4\text{H}_9 \cdot \text{NH}_2 = 441.0$ .

A white powder containing the equivalent of 53% of  $\text{Bi}_2\text{O}_3$  and 17% of As. Prepared by interaction between bismuth sodium tartrate and sodium arsenate. It is best given as a suspension of the freshly precipitated compound containing 1 grain (0.06 g.) in 15 minims (1 ml.).

**Dose.**—Intramuscularly for adults 2 to 3 ml., for grown-up children 1 ml., for young infants 0.5 ml.

For use in syphilis and yaws.

**Quinine Iodobismuthate** (*Fr. Cx., P. Belg. IV, F.E. VIII*).  $(\text{BiI}_3)_2, \text{C}_{20}\text{H}_{24}\text{N}_2\text{O}_2, 2\text{HI} = 1759.74$ .

A bright red powder *insoluble* in water. Decomposed slowly on prolonged contact with water. Contains about 23% of Bi, 57% of I and 18% of quinine.

For intramuscular injection as a suspension in sterile oil in syphilis, usually in conjunction with arsenicals. Its action is less rapid and more prolonged than that of other bismuth injections. It is especially indicated in cases with a persistent Wassermann reaction resistant to the arsphenamines. Contraindicated in pulmonary tuberculosis and the following when *not* due to syphilis: advanced diseases of the heart and nervous system, nephritis, severe diabetes, cachexia.

**Suspension d'Iodobismuthate de Quinine (Fr. Cx.).**

Sterilise the pestle and mortar by burning a little spirit in the latter, and incorporate quinine iodobismuthate 17 g. with anhydrous wool fat 5 g., and neutral olive oil 87 g., making up to 100 ml. 1 ml. contains approx. 0.04 g. of Bi.

**Bismosalvan (Richter, London), Quinostab (Boots, Nottingham), Spirobismol (Camden Chemical Co., London) and Rubyl (Pharmaceutical Specialities (May & Baker) Ltd., London)** are 10% suspensions of quinine iodobismuthate in olive oil. *Average dose.*—3 ml. by intramuscular injection once or twice weekly for a course of 15 to 24 injections.

**Neobismosalvan (Richter, London) and Spirobismol S.S. (Camden Chemical Co., London)** are similar preparations containing also lecithin.

**Sodium Iodobismuthite.** *Syn.* SODIUM BISMUTH IODIDE.

A red crystalline compound consisting chiefly of hydrated  $\text{Na}_2\text{BiI}_4$ . Prepared by the interaction of bismuth iodide or chloride with dry sodium iodide in anhydrous ethyl acetate solution. Contains about 21% of Bi. *Soluble* 1 in 1 of water, giving a black precipitate of bismuth iodide on diluting and a red precipitate of oxyiodide on further diluting. For use in syphilis. It is claimed that it appears in the spinal fluid and penetrates the brain tissue.

*Preparation of sodium iodobismuthite.*—P. J. Hanzlik *et al.*, *J. Amer. med. Ass.*, 1/1932, 537.

**Iodobismutol with Saligenin (Squibb, New York; Savory & Moore, London).** 2 ml. ampoules containing a solution of sodium iodobismuthite 0.12 g., sodium iodide 0.24 g., saligenin 0.08 g. (as local anæsthetic), in propylene glycol. *Suggested dose.*—2 ml. intramuscularly two or three times weekly for 12 injections.

Found as efficacious as any bismuth compound hitherto tried.—G. C. Johnson *et al.*, *J. Pharmacol.*, 1932, 45, 469.

In laboratory animals the bismuth enters the brain in from 90 to 100% of cases, and it is claimed that it will penetrate the brain in significant quantity in a great majority of persons, though this requires further confirmation.—*N.N.R.*, 1940.

**Bismuthi Hydroxidum.** *Syn.* BISMUTHUM HYDROXYDATUM, HYDRATED BISMUTH OXIDE.

*Dose.*—5 to 20 grains (0.3 to 1.2 g.).

A yellow (partly hydrated) or white (hydrated) bismuth oxide usually containing a large proportion of carbonate.

*Insoluble* in water. Soluble in acids and in alkalis in presence of glycerin.

*Uses.* A substitute for bismuth carbonate; also injected intramuscularly in syphilis.

**Mistura Bismuthi Hydroxidi (B.P.C.).** *Syn.* MAGMA BISMUTHI.

*Dose.*—1 to 2 drachms (4 to 8 ml.).

A suspension of freshly precipitated hydrated oxide, free from carbonate, containing the equivalent of 10% w/v of  $\text{Bi}_2\text{O}_3$ . The precipitated hydrate loses water when stored for a few weeks and becomes yellow and dense.

Does not liberate carbon dioxide in the stomach.

**Mistura Bismuthi et Magnesii Hydroxidum (B.P.C.).**

*Dose.*—1 to 2 drachms (4 to 8 ml.).

Equal parts of mixture of bismuth hydroxide and mixture of magnesium hydroxide.

The magnesium hydroxide counteracts the constipating effect of the bismuth hydroxide.

**Bismosal (Arnfield & Sons, Stockport).** *Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.). Children 5 to 20 minims (0.3 to 1.2 ml.). Contains bismuth as hydroxide in suspension with salol. In diarrhoea.

**Casbis (Bayer Products, London).** Oily suspension of bismuth hydroxide (10% Bi). *Dose.*—0.5 to 1 ml. by intragluteal injection.

**Muthanol (Bengué, London).** Suspension of bismuth hydroxide and mesothior bromide in olive oil for intramuscular injection in syphilis.

**Thio-bismol.** *Syn.* SODIUM BISMUTH THIOGLYCOLLATE.

*Dose.*—3 grains (0.2 g.) intramuscularly, dissolved in 1 ml. of sterile distilled water.

Thio-bismol is obtained by the interaction of sodium thioglycollate and bismuth hydroxide. It has the approximate formula  $\text{Bi}(\text{SCH}_2\text{CO}_2\text{Na})_3$ , and contains about 38% of Bi. Thio-bismol is a yellow, hygroscopic, granular substance with an alliaceous odour.

Freely *soluble* in water, but the solution is unstable and must be prepared immediately before use.

**Uses.** For the treatment of those cases of syphilis in which it is desirable to saturate the patient with bismuth quickly. It is stated to produce little or no pain at the site of injection and to be rapidly absorbed. The usual dose, given by deep intramuscular injection, is 0.15 to 0.2 g., the injections being given twice weekly for ten to twelve doses.

**THERAPEUTIC MALARIA.** Thio-bismol is a reliable drug in the treatment of therapeutic malaria, and by its use many untoward malarial results can be avoided. Moreover, where it is desired to terminate a course of therapeutic malaria without shock to the patient, it will be found that an intramuscular injection of thio-bismol, plus quinine or Atebrin by the mouth, will accomplish this.—H. N. Cole *et al.*, *J. Amer. med. Ass.*, ii/1940, 422.

Sodium bismuth thioglycollate may be usefully employed to smooth the shock of therapeutic malaria while increasing its non-specific therapeutic effect, by means of sharp paroxysms properly spaced, and permits of an increase in the total number that may be given. The general strength of the patient is thus conserved and his period of convalescence shortened. Experience shows that single doses of 0.1 g. intramuscularly exert a definite controlling influence on the sequence of the malarial spasms.—L. A. Brunsting and W. R. Love, *Proc. Mayo Clin.*, 1940, 285.

**Bismuthi Naphtholas (B.P.C.).** *Syn.* NAPHTHOL-BISMUTH, BASIC BISMUTH BETANAPHTHOLATE.  $\text{Bi}_2\text{O}_3(\text{OH})\text{C}_{10}\text{H}_7\text{O} = 610.1$ .

*Dose*.—5 to 15 grains (0.3 to 1 g.) in a cachet.

A pinkish-brown almost tasteless odourless powder, insoluble in water, slightly soluble in alcohol 90%.

A useful antiseptic and astringent for the stomach and intestines. Externally as a dusting powder for skin diseases and ulcers.

**Bismuthi Nitratis Crystallisatus** (*Fr. Cx., P.G. VI*). *Syn.* BISMUTHI NITRAS NEUTRUS (*F.E. VIII, P. Ital. V*).

$\text{Bi}(\text{NO}_3)_3 \cdot 5\text{H}_2\text{O} = 485.1$ .

*Dose*.—5 to 10 grains (0.3 to 0.6 g.).

In colourless deliquescent crystals, which, if dissolved in a small quantity of water, give a solution with an acid reaction; this on further dilution throws out basic bismuth subnitrate. It is practically insoluble in alcohol 90%, but soluble in cold glycerin, *cf.* Glycerinum Bismuthi Nitratis *infra*. It is astringent and antiseptic, and useful for the diarrhoea of phthisis.

**Glycerinum Bismuthi Nitratis.**

Bismuth nitrate in crystals 1, glycerin to 4. Diluted 4 or 5 times with glycerin is a stimulant application in eczema and for chapped hands.

**Bismuthi Oxidum** (*B.P.C.*).  $\text{Bi}_2\text{O}_3 = 466.0$ .

*Dose*.—5 to 20 grains (0.3 to 1.2 g.).

Is prepared by boiling bismuth subnitrate in solution of sodium hydroxide, washing and drying the deposited yellowish bismuth oxide. May be precipitated with acid from an alkaline solution containing glycerin.

**Anderson's Ointment.**

Bismuth oxide 1, oleic acid 8, white wax 3, white soft paraffin 9. In pruritus.

**Bismuthi Oxyiodogallas** (*B.P.C., P. Jap. V, P. Helv. V, P. Ned. V, P.G. VI*).  $\text{C}_6\text{H}_2(\text{OH})_3\text{COOBi} \cdot \text{OH} \cdot \text{I} = 521.7$ .

*Syn. and Prop. Name.* BISMUTH OXYIODOSUBGALLATE, AIROL (*Roche Products, Welwyn Garden City*), AIROFORM, AIROGEN.

A light greyish-green powder, odourless, tasteless, and non-irritant. It darkens on exposure to air. *Insoluble* in water, alcohol and ether. Used as ointment for ulcers, boils, whitlows, chancres, and intertrigo. Also as dusting powder, *e.g.*, for gonorrhoeal ophthalmia.

**Anusol Suppositories** (*Warner, London*). Oil of theobroma 5.87, wool fat 7.86, magnesium stearate 0.5, boric acid 18.38, zinc oxide 10.91, kaolin 2.33, bismuth resorcinate 1.77, bismuth oxyiodogallate 2.25, methyl violet B 0.04, castor oil 3.98, balsam of Peru 3.10, soft paraffin to 100. For hæmorrhoids.

**Bismuthi Phenas.** *Syn.* PHENOL-BISMUTH.

*Dose*.—5 to 20 grains (0.3 to 1.2 g.).

A white powder, insoluble, containing a variable amount of phenol, combined with bismuth oxide. Acts slowly on the digestive tract and does not cause carboluria.

The exact formula of the compound is uncertain. Products with the highest phenol content are obtained by precipitation from neutral solution in the cold. The figures do not agree with  $\text{Bi}(\text{OH})_3 \cdot \text{C}_6\text{H}_5\text{O}$ .

**Bismuthi Salicylas** (*B.P., U.S.P. XI, P. Helv. V, P.G. VI, P. Ital. V, P. Dan., P. Belg. IV, P. Ned. V, P. Jap. V, Fr. Cx.*).

*Syn.* BISMUTH OXYSALICYLATE, or SUBSALICYLATE. The formula approximates to  $\text{C}_6\text{H}_4 \cdot \text{OH} \cdot \text{COO} \cdot \text{BiO} = 362.0$ .

**Dose.**—10 to 30 grains (0·6 to 2 g.) orally; 1 to 2 grains (0·06 to 0·12 g.) by intramuscular injection.

A white, micro-crystalline powder, *insoluble* in water, alcohol, and glycerin, yielding on incineration about 64% of  $\text{Bi}_2\text{O}_3$ . It is decomposed in the presence of alkali bicarbonates with effervescence. Useful internally *per os* in some forms of diarrhœa, typhoid fever and gastric catarrh, and as a substitute for iodoform. A good intestinal antiseptic. Is given intramuscularly in syphilis in oily suspension, and has been advocated in the treatment of yaws, eight injections at weekly intervals being usually sufficient to effect a cure.

### **Injectio Bismuthi Salicylatis (B.P.).**

**Dose.**—10 to 20 minims (0·6 to 1·2 ml.) by intramuscular injection.

Contains 10% *w/v* of bismuth salicylate suspended in a sterile solution of camphor 1%, and phenol 1%, in olive oil.

**B.P. Add. III** allows the use of arachis oil, in place of olive oil, in making injection of bismuth salicylate.

**LICHEN PLANUS.** Usually cured by a course of 10 to 12 weekly intramuscular injections of  $1\frac{1}{2}$  grains bismuth salicylate in olive oil.—H. D. Grossman, *per J. Amer. med. Ass.*, ii/1932, 1203.

**Bisantol (Pharmaceutical Specialities (May & Baker) Ltd., London).** Suspension of bismuth salicylate in oil for intramuscular injection containing 0·057 g. of Bi per ml.

**Mesuroil (Bayer Products, London).** Basic bismuth methoxyhydroxybenzoate. Administered intramuscularly as a 20% emulsion in the treatment of syphilis.

**Bismuthum Subsalicylicum, Basic (Fr. Cx.).**

$\text{C}_6\text{H}_4\text{·OH·COO·Bi(OH)}_2 = 380\cdot1$ .

**Dose.**—5 to 20 grains (0·3 to 1·2 g.).

An amorphous anhydrous insoluble white powder neutral to litmus, incompatible with acids.

### **Bismuthi Oxychloridum (B.P. Add. I).**

**Syn. BISMUTH SUBCHLORIDE (B.P.C.).**  $\text{BiOCl} = 260\cdot4$ .

**Dose.**—10 to 30 grains (0·6 to 2 g.); by intramuscular injection,  $1\frac{1}{2}$  to 3 grains (0·1 to 0·2 g.).

An amorphous or minutely crystalline powder *insoluble* in water, soluble in dilute acids. Pearl white or "*blanc de perle*" is bismuth subchloride precipitated by adding hydrochloric acid to a solution of the nitrate; "*blanc d'Espagne*" or flake white is precipitated with sodium chloride.

Given internally it produces a coating on the irritated parts of the stomach or bowels. As insufflation to the larynx  $\frac{1}{4}$  to 1 gr.

Intramuscular injections have given good results in the treatment of lupus erythematosus.

**LUPUS ERYTHEMATOSUS.** The best tolerated salt of bismuth is the oxychloride suspended in water, with chlorbutol added to relieve pain on injection. The patient should be kept under a heavy bismuth dosage for 10 or 12 weeks, injections equivalent to 0·2 or 0·3 g. of bismuth being given once or twice weekly to a total of 3 or 4 g. in a series of 10 or 12 injections. After an interval of 6 weeks another course may be given.—R. M. B. MacKenna, *Med. Pr.*, 1935, 248.

**SYPHILIS.** Bismuth oxychloride preferred in syphilitic treatment. It is probably reduced to metal. Course of 4 g. in 10 injections. Give *concurrently*



with arsphenamine, rather than bismuth or mercury to follow. Quinine iodo-bismuthate has disadvantage of low bismuth content.—L. W. Harrison, *Lancet*, i/1930, 764.

**Injectio Bismuthi Oxychloridi (B.P. Add. I).**

*Dose.*—15 to 30 minims (1 to 2 ml.), by intramuscular injection.

Bismuth oxychloride 10% w/v with dextrose and cresol in sterilised water.

**Mucilago Bismuthi.** For X-ray diagnosis.

Bismuth oxychloride  $1\frac{1}{2}$  to 2 or 3 ounces or more made into a thick paste with acacia mucilage for a dose, for determining condition of the œsophagus and for examining shape, position and motor function of the stomach. A special bismuth oxychloride free from nitrate is made for X-ray work. It is inert in the stomach.

Bismuth in bread and milk in proportion of  $1\frac{1}{2}$  oz. of bismuth oxychloride to  $\frac{1}{2}$  pint of bread and milk to form a thick paste—not a liquid—is also employed and is in some respects more suitable.

In tuberculous joints bismuth injections are useful for diagnosis and treatment.

See also Bismuthi Carbonas *antea*, and *Radiology*, Vol. II.

**Unguentum Bismuthi Oxychloridi.**

Bismuth oxychloride 1, white soft paraffin 15.

Is useful for anointing the speculum for vaginal examinations.

**B.C.C. Dusting Powder** (*Blythswood Chemical Co., Glasgow*) contains bismuth oxychloride, talc, light magnesium carbonate and boric acid. For nursery and general use.

**Bismurung** (*Blythswood Chemical Co., Glasgow*). An ointment of bismuth oxychloride 10% in colloidal dispersion, for chronic lupus erythematosus, rubbed in for at least 2 minutes twice daily. Also for general use as a sedative and antiseptic ointment. Also issued as pessaries and suppositories. **Bismurung-Tropical** is the same as Bismurung, but has the melting point of the base adjusted to make it suitable for tropical climates. It is of value in "prickly heat." **Suspensol Bismuth Cream.** A colloidal bismuth preparation containing  $7\frac{1}{2}\%$  of Bi, for the administration of bismuth by inunction. *Dose.*—20 to 40 grains daily for 30 to 40 days. For the treatment of congenital syphilis in infants, 5 to 10 grains daily.

Pustular folliculitis cleared up; tinea unguium and chancroids also treated. May be of value in yaws.—R. M. B. MacKenna, *Lancet*, i/1931, 126.

**Bisoxyl** (*British Drug Houses, London*). A suspension of bismuth oxychloride in chlorbutol solution containing 0.1 g. per ml. Initial dose 0.1 g., increased to 0.2 g., corresponding to 0.01 and 0.02 g. of the bismuth salt. For syphilis and yaws.

**Chlorostab** (*Boots, Nottingham*). Bismuth oxychloride suspension in isotonic glucose solution in two strengths: 1 ml. = 0.16 g. of Bi metal and 1 ml. = 0.2 g. *Dose.*—1 injection (= 0.40 g. of Bi) intramuscularly per week for 10 weeks; or 2 injections (each = 0.20 g. of Bi) per week for 10 weeks. *Dose* for children according to age and body weight, e.g., from 1 to 4 years the equivalent of 0.05 g. of Bi metal; from 4 to 8 = 0.06 to 0.07 g. Bi metal; over 8 years = 0.10 to 0.20 g. In syphilis, congenital syphilis, etc.

**Bismuthi Subgallas** (*B.P.C., U.S.P. XI, P. Helv. V, Fr. Cx., etc.*).  $C_6H_2(OH)_3CO \cdot O \cdot (BiO)_2H_2O$  or  $Bi(OH)_2C_7H_5O_5 = 412.1$ . *Syn. and Prop. Name.* BISMUTH OXYGALLATE, BASIC BISMUTH GALLATE, DERMATOL (*Bayer Products, London*).

*Dose.*—10 to 30 grains (0.6 to 2 g.).

**Manufacture.** Bismuth carbonate 258 and gallic acid 188 are heated in presence of water 2000, until interaction has occurred.

The *Fr. Cx.* method is also satisfactory: Dissolve bismuth nitrate *cryst.* 100 g. in glacial acetic acid 200 g. Dilute with water 500 ml. and add with stirring gallic acid 37 dissolved in water 1500 ml. Wash the ppt. until the liquor is no longer acid to litmus. Dry at not exceeding 60°. *P. Ital.* method is similar. It may also be prepared by the action of gallic acid on freshly precipitated bismuth hydroxide.

An odourless, yellow, **insoluble**, non-irritant antiseptic dusting powder, employed alone or with starch.

**Incompatible** with alkaline sulphur compounds.

**Uses.** Given internally for diarrhoea in doses of 30 to 90 grains daily. Emulsion of bismuth subgallate 2, acacia 2, water 25, has been used in gonorrhoea, with good results.

In ulcerative colitis an emulsion may be used to adhere to the mucosa and a 5% suspension in olive oil is also stated to give good results; also of value after pile operations. Promotes healing.

Collapsible tubes, with catheter attachment, of bismuth subgallate ointment (10%), with paraffin basis, are useful in gonorrhoea; this ointment is also good for burns and eczema.

**DYSENTERY.** Rectal injections of bismuth subgallate 5%, in olive or cod-liver oil are much used in amoebic and chronic bacillary dysentery. In the preparation, suspending agents must not be used, and slow and thorough grinding is the best method. Before use the suspension must be thoroughly stirred and then well shaken. The dose varies between 4 and 10 ounces daily.—O. Turner, *Trans. R. Soc. trop. Med. Hyg.*, 1940, 34, 112.

**Carbasus Bismuthi Subgallatis.** BISMUTH SUBGALLATE GAUZE.

To prepare, use an emulsion of bismuth subgallate,  $\frac{1}{2}$  to 1 of glycerin to 2 of alcohol (90%) and proceed in the customary manner—the final strength being 10 to 20% of bismuth in the gauze as required. For packing cavities.

**Suppositorium Bismuthi Subgallatis (B.P.C.).** 5 grains.

**Suppositorium Bismuthi Subgallatis Compositum**

(B.P.C.). *Syn.* SUPPOSITORIIUM BISMUTHI ET RESORCINI COMPOSITUM.

Bismuth subgallate 3 gr., resorcinol 1 gr., zinc oxide 2 gr., and balsam of Peru 1 m. in each suppository.

[P1] B.F.L. (*Sharp & Dohme, London*). Bismuth-formic-iodide compound. Bismuth-formic-iodide 70 gr., acetanilide 30 gr., zinc sulphocarbolate 10 gr., bismuth subgallate 20 gr., powdered alum 3 gr., boric acid 128 gr. Antiseptic dusting powder for wounds, eczema, etc.

**E.D.P.** (*Evans, Sons, Lescher & Webb, Liverpool*). Bismuth formic iodide as surgical dusting powder.

**Bismuthi Subnitrates (B.P.C., P. Ned. V, P. Helv. V, P. Ital. V, P.G. VI, P. Dan., U.S.P. XI, P. Jap. V, Fr. Cx.).** *Syn.* BISMUTH OXYNITRATE, MAGISTERIUM BISMUTHI.

**Dose.**—5 to 20 grains (0.3 to 1.2 g.).

A white microcrystalline powder, containing 79 to 81% of  $\text{Bi}_2\text{O}_3$  obtained by precipitating a bismuth nitrate solution with alkali. Composition corresponds to  $6\text{Bi}_2\text{O}_3 \cdot 5\text{N}_2\text{O}_5 \cdot 9\text{H}_2\text{O}$ . The oxysalt,  $\text{BiONO}_2 \cdot \text{H}_2\text{O}$ , obtained by precipitation of bismuth nitrate solution with water, contains about 76% of  $\text{Bi}_2\text{O}_3$ .

**Insoluble** in water and alcohol; soluble in nitric and hydrochloric acids.

**Incompatible** with alkaline carbonates, also decomposes potassium iodide, and incompatible with tannin and sulphur.

Best suspended in aqueous vehicle by compound tragacanth powder, 1 dr. to 8 oz., or by powdered acacia or with half its weight of starch powder.

**Uses.** In gastric ulcer and dysentery as an intestinal antiseptic, and occasionally as a dusting powder in eye work. By virtue of its continuous nitrite action it has been suggested for use in hypertension, in a dose of 10 grains three times daily. For the treatment of wounds it is used with iodoform in the form of "B.I.P.P."

Gastric ulcer may be treated by bismuth subnitrate rubbed into a paste with liquid paraffin. Decomposition into nitrite in the stomach is avoided, *cf.* Bismuth Carbonate.

**HYPERTENSION.** Following the administration of bismuth subnitrate by mouth, the nitrite content of the blood is increased by three or four times the normal concentration. This increase in nitrite concentration is associated with a fall in the arterial tension. Reduction of the arterial tension does not invariably follow taking bismuth subnitrate by mouth, but in such instances there is no increase in the nitrite content of the blood. Thus a parallelism between the nitrite content of the blood and the arterial tension has been shown. The experimental evidence confirms the clinical impression that following the oral administration of bismuth subnitrate, small amounts of nitrite are slowly and continuously absorbed from the bowel.—E. J. Stieglitz and A. E. Palmer, *J. Pharmacol.*, 1936, 50, 222.

**SYPHILIS.** Bismuth subnitrate as effective as any other bismuth compound. Good results with following injection: Bismuth subnitrate 10 g., Novocaine nitrate 1 g., sterile almond oil 100 g., the dose being 1 ml. (0.07 g. of bismuth) every third day.—E. Sonnenberg, *per Prescriber*, 1926, 329.

**Enema Bismuthi et Sodii Salicylatis.**

Bismuth subnitrate 3 dr., sodium salicylate 2½ dr., psyllium seed mucilage to 1 pint.

**COLITIS**, the treatment of, by Revelliod's method (modified).

Empty the bowels by enemata of warm water twice daily for three days—on the fourth day inject the above. Action of the bowels must be discouraged after the injection, as the medicament should be retained for two days, if possible, to permit of absorption.

During the injection the patient should lie upon the left side with the pelvis raised 2 or 3 inches. This treatment has, of course, no effect upon enteritis alone or complicating (? originating) colitis; consequently a modification is necessary.

### D-P1-81] *Insufflatio Bismuthi et Morphinae (B.P.C.).*

*Syn.* FERRIER'S SNUFF.

Bismuth subnitrate 75% and morphine hydrochloride 0.4% in powdered acacia.

From 1 to 2 drachms may be used in 24 hours as snuff for catarrh. For acute coryza add powdered cubebs. It may cause drowsiness for some hours in susceptible patients.

**Injectio Bismuthi Subnitratis.**—BECK'S BISMUTH PASTE. For X-ray examination of fistulae (*cf.* also Bismuthi Subchloridum).

It sometimes causes toxic symptoms after application. If this occurs, remove dressing, wash out wound. Give morphine, ½ gr. hypodermically, if cramps in limb are severe.

(a) For DIAGNOSIS AND EARLY TREATMENT. Place bismuth subnitrate 1 in a mortar sterilised by burning a little spirit in it and add in portions hot melted white soft paraffin 2.

(b) For LATE TREATMENT. Bismuth subnitrate 6, white wax 1, hard paraffin 1 (m.p. 120°F.), white soft paraffin 12. Prepare on similar lines to the last.

The (a) form was originally injected to diagnose the extent of chronic tuberculous sinuses. It was found also to have curative effect. It is melted before use. The (glass) syringe must be sterilised dry and the plunger dipped in sterile oil before charging.

The following is a modification:—Bismuth oxychloride 1, white soft paraffin  $1\frac{1}{2}$ , liquid paraffin  $1\frac{1}{2}$ , for injection into sinuses.

By X-ray examination, sinuses can be localised. Large quantities should not be left *in situ*.

Three ounces of (a) injected at the knee, and later 4 ounces further caused poisonous effects. Caution is necessary when using for diagnostic purposes.

The bismuth is bactericidal, chemotactic and astringent. Mechanical action is also good.

### **Pasta Bismuthi et Iodoformi (B.P.C.). Syn. B.I.P.P.**

Bismuth subnitrate 25, iodoform 50, liquid paraffin 25 (by weight).

Large infected wounds have been treated without special drainage, the paste being applied as a thin covering over the wounded surface, which is then dressed in the usual way. Wounds can be closed by sutures at any period and the dressings can be left on one to six weeks. It is said to give excellent results in the treatment of acute osteitis.

POISONING in a girl of 8 following the use of 1 ml. of the paste after swabbing the wound with ether. Rapid pulse-rate, high temperature and dry skin, vomiting, diarrhoea and delirium. Recovery after irrigations of wound with 10% sodium bicarbonate solution, glucose per rectum and salines intravenously.—R. C. Shaw, *Lancet*, i/1933, 250.

OSTEITIS. Gives excellent results in the treatment of acute osteitis. There is a low mortality rate, complications are few and the average period of hospitalisation short. The late results concerning growth and function are excellent. Frequent dressings are avoided and the dressings themselves are painless.—J. H. Saint, *Lancet*, i/1937, 1263.

TROPICAL ULCER well treated.—T. R. E. Kerby, *Lancet*, i/1932, 237.

B.I.P.P. modified. Bismuth subnitrate 1, iodoform 2, and soft paraffin 13. Good in appendicitis operations, but some say it should never be introduced into the vagina.—R. A. Stoney, *Brit. med. J.*, ii/1930, 737.

The following formula is an improvement on the one containing 25% paraffin: bismuth subgallate 4 oz., iodoform 8 oz., liquid glucose  $3\frac{1}{2}$  oz., balsam of Peru 4 dr. During the war of 1914-1918 this was used with almost never-failing success. The process is: (1) a clean dissection of the damaged and infected tissues, (2) a liberal smearing or filling up with B.I.P.P. The wound granulates from below upwards and needs no further dressing.—A. Priestman, *Brit. med. J.*, ii/1939, 1164.

[D-P1-81] Unguentum Bismuthi et Cocainæ (St. Mark's H.).

Bismuth subnitrate 120 gr., cocaine hydrochloride 8 gr., white soft paraffin to 1 oz.

Bismocarbon (Richter, London). Tablets contain bismuth subnitrate 4 gr. and charcoal 4 gr. In dysentery, gastro-enteritis, etc.

Bisodol (Bisodol, London). Bismuth subnitrate, magnesium carbonate, sodium bicarbonate, carica papaya, diastase, oil of peppermint. Dose.—One level teaspoonful in water. Antacid.

### **Bismuthi Tannas. Syn. BISMUTUM BITANNICUM (P. Helv. V).**

Dose.—5 to 30 grains (0.3 to 2 g.).

A brownish-yellow powder insoluble in water. Is astringent, and useful in diarrhoea and dysentery.

## BROMUM

*B.P.C., P. Jap. V.*

Br = 79.9.

A dark brown liquid, sp. gr. about 3.14, with penetrating odour.

**Soluble** 1 in 30 of water *w/w*; readily soluble in organic liquids with gradual decomposition of the solvents. Is not used as such medicinally.

**Antidotes.** Emetics sometimes useful. Inhalations of very dilute ammonia, also of alcohol. Keep patient in fresh air. Give milk, white of egg or starch mucilage. Steam inhalations sometimes useful. Oxygen inhalations. Atropine,  $\frac{1}{100}$  gr., hypodermically. Venesection and blood transfusion may be necessary.

**Bromal Hydras.**  $\text{CBr}_2\text{CH}(\text{OH})_2$  = 298.8.

*Dose.*—2 to 5 grains (0.12 to 0.3 g.) at bedtime.

In large colourless crystals, which melt on the hand, soluble in water 1 in 2½. Applied externally it irritates the skin. It has been tried in epilepsy, chorea and insomnia.

**Brom-Albumen.** *Syn.* BROMO-PROTEIN.

*Dose.*—10 grains (0.6 g.) = ½ gr. of bromine approx.—increased as desired.

Contains 7% of bromine, combined with albumen. Made by interaction of bromine with egg albumen, in form of a light brown powder. As a substitute for alkali bromides in epilepsy, where larger doses than the above may be required. It is hardly soluble in 0.2% hydrochloric acid, even in presence of pepsin, but is readily dissolved in 0.5% sodium bicarbonate in the presence of pancreatin, hence absorption takes place in the intestines.

**Multibral** (*Napp, London*). Sodium monobromoleate. Coated pellets contain 0.03 g. of bromine. *Dose.*—1 to 3 pellets thrice daily. For intensified bromine action with freedom from secondary effects.

**Bromoformum** (*B.P.C., P. Helv. V, Fr. Cx., P. Ital. V, P. Ned. V, P. Belg. IV, F.E. VIII*). *Syn.* TRIBROMOMETHANE.  $\text{CHBr}_3$  = 252.8.

*Dose.*—½ to 2 minims (0.03 to 0.12 ml.) or more. *P.G. VI* and *Fr. Cx.* have maximum single dose 0.5 g.; maximum during 24 hours 1½ g. (= 8 minims approx.). Children as many drops as years old—up to 6.

A heavy, limpid, colourless, sweet liquid, with an agreeable odour; sp. gr. about 2.63. Distils mainly between 148° and 155°.

**Soluble** 1 in 800 of water, 1 in 80 of glycerin. Miscible with alcohol 90%, chloroform, ether and fixed and volatile oils. It should be preserved by addition of 0.5 to 1% alcohol. *B.P.C.* contains 3 to 4%. Is a powerful sedative, useful in insane cases. Capsules contain ½ minim (0.03 ml.) dissolved in oil. Has been employed as an antispasmodic in whooping-cough in a dose of 1 to 3 minims on a piece of sugar.

**Elixir Bromoformi** (*B.P.C.*). *Syn.* MISTURA BROMOFORMI COMPOSITA.

*Dose.*—½ to 2 drachms (2 to 8 ml.).

Bromoform 1 in 50, with alcohol 90%, tincture of orange, compound tincture of cardamom and glycerin.

**Syrupus Bromoformi.**

*Dose.*—½ to 1 ounce (8 to 30 ml.) = ½ to 2 minims of bromoform. To be diluted with an equal quantity of water or more, *at time of taking*.

Bromoform 2 m., alcohol (90%) 80 m., syrup 160 m., glycerin  $\frac{1}{2}$  oz.

The Sirop of the *Fr. Cx.* is bromoform 1, alcohol (90%) 9, glycerin 30, syrup 160.

**Uses.** In whooping cough diminishes number, duration and severity of attacks, and mucous secretion is more easily got rid of.

[P1] **Syrupus Bromoformi Compositus (B.P.C.).**

**Dose.**—1 to 4 drachms (4 to 16 ml.).

1 dr. contains about  $\frac{1}{11}$  m. of bromoform,  $\frac{1}{8}$  gr. of codeine and  $\frac{1}{8}$  m. of tincture of aconite.

[P1] **Syrupus Bromoformi Compositus (P. Ital. V).**

20 g. contains 0.02 g. of bromoform, 0.01 g. of codeine, and 0.04 g. of aconite tincture. *Fr. Cx.* is similar but contains 0.1 g. of aconite tincture in 20 g.

**Alcohol Tribromoethylicum (B.P. Add. III).**

$\text{CBr}_3 \cdot \text{CH}_2 \cdot \text{OH} = 282.8$ .

[P1] and [81] **"Tribromethyl alcohol."**

**Dose.**— $\frac{1}{2}$  to  $\frac{3}{4}$  grain per pound bodyweight (0.075 to 0.1 g. per kilogramme bodyweight), by rectal injection as a basal anæsthetic.

Tribromoethyl alcohol is a white, crystalline powder obtained by reducing tribromoacetaldehyde and into which it decomposes on heating.

**Soluble** about 1 in 35 of water; readily soluble in amylene hydrate and light petroleum. Aqueous solutions are unstable. Solutions in amylene hydrate are used as basal anæsthetics (*see* Bromethol).

[P1-81] **Bromethol (B.P. Add. III). Syn. and Prop. Name.**  
SOLUTION OF TRIBROMOETHYL ALCOHOL, AVERTIN (*Bayer Products, London*).

**Dose.**— $\frac{1}{2}$  to  $\frac{3}{4}$  minim per pound bodyweight (0.075 to 0.1 ml. per kilogramme bodyweight) *per rectum*.

Bromethol is administered in a 2.5% solution in distilled water, prepared by warming the requisite quantity of distilled water to about 37°, adding the measured amount of bromethol slowly and shaking until dissolved. The temperature must not be allowed to rise above 40°. Solutions should be freshly prepared before use and tested by the addition of a few drops of congo-red indicator to a small portion of the solution. Only those solutions giving a red or orange-red colour should be used; if a blue colour develops the solution must be discarded.

Bromethol is tribromoethyl alcohol 66.7 g., amylene hydrate 33.3 g. 1 ml. contains 1 g. of tribromoethyl alcohol.

**Soluble** 3 in 100 of water at 37°.

**Stability of Solutions.** They may be used up to 4 days if kept at room temperature. When dispensed in vacuum flasks, should be used in a few hours. Solutions to be stored should be prepared below 38° and allowed to cool immediately.—*E. H. Watson, Pharm. J., i/1938, 643.*

**Storage.** In a well-stoppered bottle protected from light, and at a temperature between 11° and 30° to prevent crystallisation or evaporation.

**Caution.** Bromethol is inflammable and volatile; care must be taken not to employ it near a flame.

**Toxic Effects.** In anæsthetic doses it has no effect on the cardiovascular system, but in larger doses it slows the rate and weakens the force of the heart-beat—the coronary vessels dilate and blood pressure falls. Toxic doses cause death by respiratory paralysis, but except for a slight transient cyanosis and a tendency to shallow breathing it has little or no effect on respiration in the doses necessary to produce narcosis. Headache and nausea and a feeling of malaise may persist for some days, but vomiting is not common.

In eight years Avertin with amylene hydrate was used at the Massachusetts General Hospital in 3934 cases. Though the use of the drug waxed and waned in this period, it was never used in more than 10% of the cases in which anaesthesia was employed. Eight factors have been chiefly responsible for the lessened use of the drug, as follows: (1) variability of response, (2) rectal irritation, (3) prolonged induction period when an inhalation anæsthetic is used as a supplement, (4) alarming immediate depression, (5) delayed effects, (6) the numerous contraindications, (7) the impossibility of efficiently removing the agent once toxic effects become evident, (8) the fatalities. Of these causes, the most important is the last—7 deaths were associated with its use. According to the mortality rate it appears to be more toxic than chloroform.—H. K. Beecher, *J. Amer. med. Ass.*, ii/1938, 122.

**Antidotes.** As an antidote for overdosage high rectal irrigation with warm hypertonic sodium thiosulphate solution acts as a restorative if applied before cardiac failure occurs. Carbon dioxide and oxygen is also of value to overcome the profound respiratory depression. Ephedrine sulphate,  $\frac{3}{4}$  to  $1\frac{1}{2}$  gr., intramuscularly or intravenously, is said to be specific, or nikethamide, 2 to 3 ml. intramuscularly. Picrotoxin, in a dose of 3 mg., is also of value.

**Contraindications.** Bromethol is contraindicated in renal disease and in cases with impaired liver function, in operations on the rectum, anus or vagina, and in the presence of inflammatory conditions of the colon and rectum. It is also contraindicated in very young or cachectic children (though children generally tolerate the drug extremely well). It should not be used in combination with respiratory depressant drugs such as morphine (except in obstetrics *vide infra*).

Three definite contraindications to the use of Avertin are: (1) whenever it is impracticable either to obtain or accurately to estimate the weight of the patient; (2) the presence of pathological condition of the rectum or colon; and (3) operations on the rectum or colon. The trend of clinical evidence seems increasingly to be that Avertin may be used with safety even in the presence of grossly damaged liver function.—H. K. Ashworth, *Arch. Dis. Childh.*, 1936, 63, 158.

**Uses.** Bromethol is mainly employed as a basal narcotic in general surgery, the requisite dose, based on the patient's weight and general condition, being run into the rectum thirty minutes before operation, from five to ten minutes being taken over the injection. The lower bowel should be emptied by an enema the night before the operation and an injection of atropine is given an hour before operation.

Generally speaking the average healthy adult is given 0.1 ml. of bromethol in  $2\frac{1}{2}\%$  solution per kilo bodyweight, but patients with high metabolic rates, such as healthy children and patients suffering from exophthalmic goitre, may be given up to 0.12 ml. per kilo bodyweight. In obese or decrepit patients, or in those

with a low blood pressure or low metabolic rate, a reduction in dose, e.g., to 0.075 ml. per kilo bodyweight, is necessary.

The patient is usually unconscious by the time administration of the solution is complete. The narcosis produced lasts for about two hours, but adequate surgical anaesthesia is usually attained by the supplementary use of nitrous oxide and oxygen. Bromethol alone rarely produces anaesthesia and it is unwise to push the dose too far. It is imperative to maintain a clear airway throughout the whole time the patient is under the effects of bromethol.

In addition to its use as a basal narcotic, bromethol is also employed for the production of "twilight sleep." For this purpose it is given at the termination of a pain in a dose of 0.075 ml. per kilo bodyweight. In the case of a primipara the os must be fully dilated and in a multipara at least three-quarters dilated, the administration being preceded by an enema to empty the rectum.

Bromethol has also been found of value, in association with tetanus antitoxin, in the control of the muscular rigidity and convulsions of tetanus.

In thyroidectomy it may be successfully employed, in the usual dose, given about 50 minutes before the operation, but it should not be given unless the pulse has previously been slowed by rest and digitalis.

**BASAL ANÆSTHESIA.** For reduction of fractures, in combination with local anaesthesia it is ideal.—B. Hughes, *Brit. med. J.*, i/1929, 898; *Lancet*, ii/1929, 1220.

Where there is serious pulmonary disease, Avertin advised; in combination with local anaesthetic or gas and oxygen it is said to be ideal.—Sir F. E. Shipway, *Brit. med. J.*, ii/1930, 663.

**Basal narcosis in children.** (Based on a series of 5918 administrations at the Booth Hall Hospital, Manchester.) The children are admitted the day before the operation. In non-abdominal cases no aperient is necessary. A simple enema is administered about 6 p.m. The evening meal should include glucose, either in the form of jam or syrup, or, each child may be given  $\frac{1}{2}$  lb. of boiled sweets. Four hours before operation a simple rectal wash-out is administered. Three hours before operation each child receives a plate of porridge or gruel, together with a liberal helping of syrup. The weight of each patient should be entered on the temperature chart, and the name, weight and required dosage of Avertin for each patient should be sent to the dispensary in writing. The usual dosage for cases in which operations are to be undertaken on the air passages, and in which a rapid return of the cough-reflex is consequently desirable, is 0.075 or 0.08 g. per kilo bodyweight. For operations other than those on the respiratory passages, a full dose of 0.1 g. per kilo should be prescribed. The bottle containing the prepared solution for each patient should bear a label stating the name and weight of the patient, the quantity of Avertin fluid and water used, and the date and hour of preparation. These particulars should be checked by the ward-nurse against those on the temperature chart before the actual administration is begun. Rigid adherence to these rules is the only adequate safeguard against the possibly disastrous results of administering the wrong dose to the wrong patient. Thirty minutes before the operation, the child is placed in the left lateral position, and the solution is run slowly into the rectum by means of a small catheter, tube and funnel. Administration should be slow, taking up to ten minutes to complete. Immediately afterwards, the child should receive a dose of atropine, graduated according to age as follows:—0-3 months, nil; 3 months-1 year,  $\frac{1}{16}$  gr.; 1-2 years,  $\frac{1}{8}$  gr.; 3-5 years,  $\frac{1}{4}$  gr.; 5-12 years,  $\frac{1}{2}$  gr.; 12 years or over,  $\frac{1}{2}$  gr. The child should then be left quiet, when it usually drops off to sleep within fifteen minutes. It is then transported to the ante-room of the operating theatre to await operation. At this stage, it can easily be roused by light stimulation, such as pinching the skin, and will invariably resist the application of a mask when the administration of ethyl chloride or



ether is begun, but amnesia is always complete.—H. K. Ashworth, *Arch. Dis. Childh.*, 1936, 63, 160.

Comparing paraldehyde and Avertin as basal narcotics for children, paraldehyde requires more patience in its administration, is less certain in its action, and requires the addition of ether to nitrous oxide and oxygen to obtain the same plane of anaesthesia as is obtained by Avertin and nitrous oxide and oxygen alone. The difference in the fall in blood pressure produced by either of the drugs is so small as to be negligible.—R. Binning, *Lancet*, ii/1937, 852.

**GENERAL ANÆSTHESIA.** Avertin can be given to children as a complete anæsthetic with safety, and approaches more nearly the ideal anæsthetic than any other. It is better than basal anaesthesia followed by inhalation anaesthesia, and is safer in children than adults. The best method is to combine 0.175 g. per kilo bodyweight with morphia and atropine according to age and 20 to 30 ml. of Novocain as a field block. A 3% solution of Avertin is better retained than a 2½%. The fall in blood pressure is not of serious moment.—J. Boyd, *Brit. med. J.*, i/1935, 1122.

**ASTHMA.** In severe asthmatic crisis, when all other methods have failed to give relief, Avertin fluid per rectum gives muscular relaxation within ten minutes (though the effect may be occasionally delayed for an hour). The patients sleep for one to six hours and on waking are usually relieved of asthma, remain so for several days or weeks, and recover their ability to respond to adrenaline injections. The dose of Avertin fluid, which is injected rectally, using a syringe or a male catheter, is 50 to 70 mg. per kilo bodyweight.—A. M. Fuchs, *J. Allergy*, 1937, 8, 340.

**GYNÆCOLOGY.** A safe drug in a dosage of 0.08 to 0.1 g. per kilo. 2000 gynaecological operations conducted without mortality or morbidity traceable to its use. Reduction of pre-anæsthetic morphine from ½ to ⅓ grain resulted in immediate lessening of respiratory depression.—J. Young and N. S. Fraser, *Brit. med. J.*, i/1934, 455.

**OBSTETRICS.** In childbirth advocated for safety, ease of administration, and mitigation of pain. It is given at second stage pains after morphine ½ grain at first (sometimes a further ½ grain). There must be 2 hours' interval between morphine and Avertin. Should be given when the cervix is fully half dilated, if the contractions are strong and regular. Some excitement may follow for 5 minutes. Dose.—0.075 ml. *Avertin Fluid per kilo weight, e.g.*, 4.5 ml. for a person of 9 stone (60 kilos), given per rectum in 1000 ml. warm water—milk has been used in preference.—Prof. Martin. The method eases pains of labour.—J. S. M. Connell, *Lancet*, ii/1930, 184.

Pleasant for the patient. Harmless to the infant. Not dangerous, but uncertain in action. More experience required to compare its merits with paraldehyde.—Gertrude M. B. Morgan, *Brit. med. J.*, ii/1932, 12.

Avertin is a dangerous drug. It should never be employed except by an expert anaesthetist. Its major drawback is its profoundly depressant action on the respiratory centre; in this respect it is even more dangerous than chloroform. In doses of over 5 mg. per kilo bodyweight it may produce uterine atony with resultant post-partum hæmorrhage. Individual variations in rate of absorption are marked, and dangerously deep narcosis may result from a moderate dose. Avertin has no place in obstetrics.—B. F. Cornwall, *New Engl. J. Med.*, ii/1939, 851.

## BUCHU

(with AGROPYRUM, etc.)

*B.P., Fr. Cx.*

The dried leaves of *Barosma betulina* (Rutaceæ); contain volatile oil and mucilage. *Fr. Cx.* allows also *B. crenulata* and similar species. Carminative and diuretic. Buchu has antiseptic action in irritability of bladder and in gonorrhœa.

**Extractum Buchu Liquidum (B.P.C.).**

*Dose.*—5 to 20 minims (0.3 to 1.2 ml.). 1 in 1, with alcohol 90%.

**Infusum Buchu Concentratum (B.P.).**

*Dose.*—1 to 2 drachms (4 to 8 ml.). 1 in 2½.

A concentrated infusion is pharmaceutically unsound, and it has been recommended that its use should be discontinued when an infusion of buchu is prescribed.

**Infusum Buchu Recens (B.P.).**

*Dose.*—1 to 2 ounces (30 to 60 ml.). 1 in 20.

In preparing this the leaves must be lightly broken and not bruised, otherwise percolation is prevented by the mucilage.—B. A. Bull, *Pharm. J.*, 1/1932, 318.

[P.] **Mist. Buchu et Hyosc. (N.I.F.).**

Potassium bicarbonate 15 gr., liquid extract of hyoscyamus 2½ m., concentrated infusion of buchu 15 m., chloroform water to ½ oz.

**Tinctura Buchu (B.P.C.).** *Dose.*—½ to 1 drachm (2 to 4 ml.). 1 in 5.

**Agropyrum (B.P.C., Fr. Cx., P. Helv. V). Syn. COUCH GRASS.**

The dried rhizome of *Agropyron repens* (Gramineæ). Contains triticin, a carbohydrate similar to inulin. Diuretic and aperient. Useful in gonorrhœa.

**Decoctum Agropyri (B.P.C.).** *Syn.* DECOCTION OF TRITICUM.

*Dose.*—½ to 2 ounces (15 to 60 ml.). 1 in 20.

**Extractum Agropyri Liquidum (B.P.C.).** *Syn.* LIQUID EXTRACT OF TRITICUM.

*Dose.*—1 to 2 drachms (4 to 8 ml.). 1 in 1.

**Extractum Agropyri Repentis (Fr. Cx.)** is a soft aqueous extract.

**Ammi Visnaga.** *Syn.* KHELLA. The fruits of *Ammi Visnaga* have diuretic properties. Preparations relax all smooth muscle, and have been given in ureteric spasm and to assist the passage of small kidney stones. Has been administered as a decoction (1 in 40, *dose.*—½ to 2 oz.) and as a tincture (1 in 10 by maceration in alcohol 90%, *dose.*—1 to 3 dr.), given thrice daily before food.

Activity is due to a crystalline principle, visammin.—K. Samaan, *Quart. J. Pharm.*, 1932, 16. See also *ibid.*, 1930, 25; 1931, 14; 1932, 186.

See also F. A. Upsher Smith, *J. Amer. pharm. Ass.*, 1933, 184.

**Chimaphila (B.P.C.). Syn. PIPSISSEWA.**

*Dose.*—15 to 45 grains (1 to 3 g.).

The dried leaves of *C. umbellata* (Pyrolaceæ). Has diuretic properties, and is used in cardiac and renal disease, being administered as Extractum Chimaphilæ Liquidum, 1 in 1, either alone or mixed with 3 parts of syrup.

**Lappa (B.P.C.). Syn. BURDOCK, BARDANE (Fr. Cx., F.E. VIII).**

Roots of *Arctium majus*, or other species of *Arctium*. Has diuretic, diaphoretic and alterative properties. On the Continent called Bardana, e.g., *Inf. Bardanæ Spirituos.* (external): Bardana 2, water (boiling) q.s. to 15, strong alcohol 5; to be rubbed into the scalp. Liquid extract 1 = 1 by diluted alcohol. *Average dose.*—30 minims. Decoction, 1 in 20. In skin affections and gout.

The use of a tincture of the seeds has largely replaced that of the root in U.S.A., especially in the treatment of psoriasis, acne and prurigo.—*Chem. & Drugg.*, 1/1925, 216.

**Maidis Stigmata** (*P. Helv. V*). *Syn.* CORN SILK.

The dried stigmas and styles of maize, *Zea Mays* (Gramineæ). Demulcent and diuretic. Used in cystitis and nocturnal incontinence of urine.

**Extractum Maidis Liquidum.** *Dose.*—1 to 2 drachms. 1 in 1.

**Syrupus Maidis.** *Dose.*— $\frac{1}{2}$  to  $\frac{1}{4}$  drachm. Liquid extract 1, syrup 9.

**Uva Ursi** (*B.P.C., P. Jap. V*). *Syn.* BEARBERRY LEAVES, BUSSESOLE (*Fr. Cx., P. Dan.*).

The dried leaves of *Arctostaphylos Uva-ursi* (Ericaceæ). Contains a crystalline glycoside, arbutin,  $C_{12}H_{16}O_7, \frac{1}{2}H_2O$ , m.p. about  $168^\circ$ . Bearberry is diuretic and astringent and exerts an antiseptic effect on the urinary tract. It is employed in urethritis, cystitis, etc.

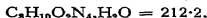
The precipitate which forms in liquid extracts of bearberry consists of ellagic acid formed by enzymic hydrolysis of ellagi-tannin. The precipitation can be prevented by heating the crude drug in an autoclave at  $110^\circ$  (5 lb. pressure) for 30 minutes on three successive days before preparing the extract. The arbutin content is only slightly affected by this procedure.—L. M. Parks and C. O. Lee, *J. Amer. pharm. Ass.*, 1937, 702, 706.

**Infusum Uvæ Ursi Concentratum** (*B.P.C.*). 1 in 2 $\frac{1}{2}$ . *Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

**Infusum Uvæ Ursi Recens** (*B.P.C.*). *Dose.*— $\frac{1}{2}$  to 1 ounce. 1 in 20.

## CAFFEINA

*B.P., U.S.P. XI, P.G. VI, P. Ned. V, Fr. Cx., P. Jap., P. Ital. V, P. Helv. V, P. Dan., F.E. VIII, P. Belg. IV.*



*Syn.* THEINE, GUARANINE, TRIMETHYLXANTHINE.

*Dose.*—2 to 5 grains (0.12 to 0.3 g.) or more—as much as 18 grains being recommended—given in solution, or in pills. *Fr. Cx.* has max. single dose 0.5 g., max. in 24 hours 2 g.

Caffeine is 1:3:7-trimethyl-2:6-dioxypurine, a crystalline alkaloid, m.p. about  $235^\circ$  to  $237^\circ$  after drying at  $100^\circ$ , usually obtained from the dried leaves of *Camellia Thea*, or dried coffee-seeds—*Coffea arabica*; also contained in guarana, maté and kola. Caffeine and theobromine (*q.v.*) can be prepared from xanthine. These are purine derivatives.

**Soluble** 1 in 80 of water, 1 in 2 of boiling water, about 1 in 40 of alcohol 90%, 1 in 9 of chloroform, 1 in 154 of benzene, and scarcely in light petroleum and ether; acids render it more soluble in water, but it is a feeble base, and on concentrating the solution of the salts they are apt to split up, and the caffeine crystallises out by itself. Is rendered soluble in less water by the addition of an equal quantity of phenazone, sodium salicylate, etc. *See also* Caffeine-Sodio-Salicylate, etc.

**Antidotes.** Empty stomach by emetic or by stomach tube, using 60 gr. of potassium permanganate in 2 gallons of water.

Give brandy,  $\frac{1}{2}$  oz., or aromatic spirit of ammonia,  $\frac{1}{2}$  dr., in water freely. Keep patient warm, especially extremities. Morphine,  $\frac{1}{2}$  gr., with atropine  $\frac{1}{10}$  gr. hypodermically. (The fatal dose of caffeine is so large that no fatal case of poisoning is on record, but doses of more than 1 g. may produce alarming symptoms.)

**Uses.** Caffeine is used as a mental, muscular and respiratory stimulant, and as a cardiac tonic and diuretic. It wards off fatigue, and is of value in nervous headache and some forms of nervous dyspepsia. It is employed as a cardiac and renal stimulant in cardiac failure, chronic nephritis and dropsy. In the form of strong black coffee it acts as an antidote against acute poisoning by morphine and alcohol.

Bronchial asthma of adults is relieved by 2 to 5 grain doses of the citrate before bedtime and again during the night.

**Neuralgic Powders.** Caffeine 1 gr., quinine hydrochloride 5 gr., phenazone 10 gr. (or phenacetin 5 gr.).

Drugs of the caffeine series have a most complex effect on the circulation of animals. They tend to raise blood pressure by stimulating the vasomotor centre, tend to lower it by dilating peripheral vessels, and also cause tachycardia through direct action on the heart muscle. In man, the net results are remarkably slight and inconstant: indeed, one of us, working with the late Prof. Cushny some years ago, found no demonstrable effects upon either the pulse rate or blood pressure of patients from even intravenous injections of caffeine citrate in ordinary doses. Such evidence shows how slight is the foundation for the wide belief in its virtues as a circulatory stimulant.—C. Hoyle and J. W. Linnell, *Practitioner*, i/1936, 96.

[P1] **Caffeine-Chloral.**

Small white granular crystals, freely soluble in water, with the taste of chloral. Is analgesic and laxative, and in hypodermic injections of 3 to 8 grains useful in constipation, painful gastric distension, sciatica, and rheumatism.

**Caffeine Citras** (*B.P.C.*, *P. Helv. V*, *F.E. VIII*).

$C_8H_{10}O_2N_4 \cdot C_3H_4(OH)(COOH)_2 = 386.3$ . *Syn.* CAFFEINA CITRATA (*U.S.P. XI*).

**Dose.**—2 to 10 grains (0.12 to 0.6 g.).

A white odourless powder obtained by combining caffeine 1 and citric acid 1 in a small quantity of distilled water and evaporating to dryness on a water bath.

**Soluble** 1 in 4 of hot water, dissociating on further dilution, with separation of caffeine, which re-dissolves in 32 of water; 1 in 22 of alcohol 90%.

**Incompatible** with potassium iodide and Spiritus Ætheris Nitrosi, iodine being liberated. The following, however, does not darken:—Potassium iodide 5 gr., caffeine base  $2\frac{1}{2}$  gr., Spiritus Ætheris Nitrosi (neutralised with ammonium carbonate) 30 m., water to 1 oz.

Also incompatible with sodium salicylate. A little sal volatile or sodium hydroxide will prevent the salicylic acid being thrown out.

**Uses.** See Caffeine.

**Caffeine Citras Effervescens** (*B.P.C.*).

**Dose.**—1 to 2 drachms (4 to 8 g.).

Contains 4% of the citrate, or about  $2\frac{1}{2}$  grains in a drachm.

**Caffeina et Sodii Benzoas (B.P.).** *Syn.* CAFFEINÆ SODIO-BENZOAS (*P. Jap. V, P.G. VI, U.S.P. XI, P. Belg. IV, P. Ital. V, P. Helv. V, P. Dan.*).

*Dose.*—5 to 15 grains (0.3 to 1 g.); 2 to 5 grains (0.12 to 0.3 g.) by injection, usually hypodermically. *U.S.P. XI* average doses 5 grains and 3 grains respectively.

Contains from 47 to 50% of caffeine. *P. Ned. V* requires 50%; *P. Ital. V* must yield 43 to 46% of anhydrous caffeine.

*Soluble* 1 in 4 of water, 1 in 40 of alcohol 90%. Warm water dissolves about 1 in 1, but caffeine separates on cooling.

*Uses.* This (and the sodium salicylate preparation *v. infra*) is employed for the parenteral administration of caffeine owing to its ready solubility.

It improves breathing and circulation and, following its use, the mind and depressed vital reflexes become active and normal. Coma, shock, collapse under anæsthesia, and poisoning from morphine and other depressant drugs treated. As stimulant for desperately ill patients 2 grain doses, *intravenously*.

HÆMOGLOBINURIC FEVER has been well treated with caffeine sodio-benzoate intramuscularly, 3 grains twice daily for 7 days and once daily for further 5 days.

*SHOCK.* For use in the event of severe Novocain reaction; caffeine 3 gr., sodium benzoate 7 gr., strychnine  $\frac{1}{10}$  gr.

**Ampulla Caffeinæ et Sodii Benzoatis (L.C.C.).** Caffeine and sodium benzoate 0.3 g. (5 gr.), sterilised water to 2 ml. (34 m.).

[*P*] **Labat's Cardiac Stimulant (Anglo-French Drug Co., London).**

Caffeine 0.25 g., sparteine sulphate 0.05 g., sodium benzoate 0.30 g., strychnine sulphate 0.001 g., distilled water to 2 ml. For counteracting fall of blood pressure during regional anæsthesia.

**Caffeina et Sodii Salicylas (B.P.C., P. Helv. V, P. Dan., P. Jap. V).** *Syn.* CAFFEINÆ SODIO-SALICYLAS.

*Dose.*—2 to 5 grains (0.12 to 0.3 g.) hypodermically, or 5 to 15 grains (0.3 to 1 g.) orally. Max. single dose *per os* 1 g., or in 24 hours, 3 g.

Evaporate to dryness caffeine 50, sodium salicylate 50, water sufficient to form a smooth paste. A white amorphous powder, containing 47 to 50% of caffeine.

*Soluble* 1 in 1 of water, 1 in 28 of alcohol 90%.

The addition of camphor to injections of caffeine sodium salicylate has been suggested. Thus to 3 ml. of pure sterile glycerin add a solution of caffeine and sodium salicylate of each 0.25 g. in water 1 ml.; then add spirit of camphor (10%) 1 ml.; 5 ml. contain caffeine 0.25 g., and camphor 0.1 g.

This salt and the corresponding cinnamate and benzoate act like digitalis, but more rapidly.

Iritis of rheumatic origin has been treated by injection into the median cephalic vein of caffeine 0.05 g. with sodium salicylate 0.5 g.

**Caffeinæ Hydrobromidum (B.P.C.).**

$C_8H_{10}O_2N_4.HBr.2H_2O = 311.1$ .

*Soluble* 1 in 50 approx.

L\*

The hydrochloride,  $C_8H_{10}O_2N_4.HCl.2H_2O = 266.6$ , and the hydriodide (unstable) are in use.

*Dose of each.*—1 to 4 grains (0.06 to 0.25 g.) or more. In transparent crystals.

Has been employed in migraine and nervous headache.

**Caffeina Iodidum.** *Syn.* CAFFEINÆ TRI-IODIDUM, CAFFEINE DI- IODO-HYDRIODIDE.  $C_8H_{10}O_2N_4.I_2.HI.H_2O = 593.9$ .

*Dose.*—1 to 3 grains (0.06 to 0.2 g.).

In prismatic black iridescent crystals, slightly soluble in water (with decomposition) and in alcohol 90%.

Has been used with success in rheumatism and gout, and for the relief of asthmatic attacks.

[P1-81] **Pilula Caffeinae Tri-Iodidi Composita** (*Billimoria*).

*Dose.*—1 early in the morning, 1 about 3 or 4 p.m., and 1 at bedtime with water, to be lessened to 2 or 1 a day as required.

Caffeine tri-iodide 2 gr., sodium aminarsonate  $\frac{1}{2}$  to  $\frac{1}{4}$  gr., valerianic acid 2 m., green extract of belladonna  $\frac{1}{2}$  to  $\frac{3}{4}$  gr., jalap extract *q.s.* (if constipated), reduced iron 1 gr. (in asthma only). For one pill or preferably gelatin capsule.

Asthma has been well treated with this compound, as also has whooping cough, using proportionately smaller doses.

**Caffeina et Sodii Iodidum.** *Syn.* IODO-CAFFEINE, SODIUM-CAFFEINE IODIDE.

*Dose.*—2 to 10 grains (0.12 to 0.6 g.).

A white odourless powder with a bitter saline taste. It may be prepared by triturating equal weights of caffeine and sodium iodide with water to form a smooth paste, and drying. Thus prepared it contains about 50% of anhydrous caffeine.

*Soluble* in cold water, more soluble in warm water.

*Uses.* It is a good diuretic, especially for prolonging the diastole in cases of enfeebled heart. It is also useful in cardiac dropsy and pleurisy with effusion, and is said not to upset digestion.

**Elixir Caffein. Iodidi** (*N.I.F.*). Caffeine and sodium iodide 5 gr., sodium iodide 5 gr., liquid extract of liquorice 5 m., chloroform  $\frac{1}{2}$  m., decoction of coffee (1 in 10 with water; boil for 1 minute, filter and adjust to volume) to 1 dr.

**Elixir Caffeinae Iodidi** (*B.V.H.*). *Syn.* CAFFEINE. Caffeine sodium iodide 5 gr., sodium iodide 5 gr., dilute hydriodic acid 5 m., decoction of coffee (3 oz. in 1 pint) 40 m., water to 1 dr. Given in asthma.

**Elixir Ephedrinae et Caffeinae** (*B.V.H.*). *Syn.* EPICAFFEINE. Is the same as the above, containing also  $\frac{1}{4}$  gr. of ephedrine hydrochloride per drachm.

**Caffedrin** (*Duncan, Flockhart, Edinburgh*). Preparation containing per fl. drachm caffeine iodide 5 gr., ephedrine hydrochloride  $\frac{1}{4}$  gr., in infusion of coffee. For asthma and chronic bronchitis.

**Eupinal** (*Cuxson Gerrard, Oldbury*). Preparation containing iodide of caffeine for use in the treatment of asthma.

**Eupnine Vernade** (*Darrasse, Nanterre; Wilcox, Jozeau, London*). Stable standardised solution of caffeine iodide (1 dr. = 0.5 g.).

*Dose.*—1 teaspoonful 2 or 3 times daily before meals. Asthma, emphysema and arteriosclerosis.

**Spiroline** (*British Drug Houses, London*). Elixir containing in each drachm 3 gr. of di-iodo-caffeine hydriodide with the soluble constituents of  $7\frac{1}{2}$  gr. of coffee. In asthma and as a cardiac stimulant.

**Caffeinae Salicylas.**  $C_8H_{10}O_2N_4.C_6H_4OH.COOH = 332.2$ .

*Dose.*—1 to 5 grains (0.06 to 0.3 g.).

White crystalline powder slightly soluble in water. Useful in migraine associated with rheumatism.

**Caffeinae Valerianas.**  $C_8H_{10}O_2N_4 \cdot C_8H_{10}O_2 = 296.2$ .

**Dose.**—1 to 3 grains (0.06 to 0.2 g.). In irregular crystals or powder, of somewhat variable constitution, usually consisting of a mixture of caffeine and valerianic acid, preferably in the proportion of 4 parts to 1. It controls hysterical symptoms, and is useful in pertussis.

**Catha Edulis.** *Syn.* KAT, KHAT, ARABIAN or ABYSSINIAN TEA.

**Dose.**—1 drachm to  $\frac{1}{2}$  ounce (4 to 15 g.) infused in about 6 to 8 ounces of hot water as required. A sprig of about 10 leaves weighing about 10 grains is chewed at a time by natives.

The shrub grows wild in Abyssinia and is cultivated for native use in Arabia.

Three alkaloids were isolated by Stockman—*Cathine* (*d*-norisoephedrine), very soluble in water, *cathinine* (less soluble) and *cathidine* (insoluble). In man they all act chiefly on the cerebrum and spinal cord, causing stimulation or much excitement according to dose, and cathine alone induces slight drowsiness at first.

The herb is a stimulant narcotic. It has been known for generations for its sustaining power. The leaves when used in an infusion in the same manner as tea or coffee, or when chewed (as by the Arabs), are stated to increase "staying power," and produce wakefulness and refreshment.

**Extractum Cathæ.** **Dose.**— $2\frac{1}{2}$  to 10 grains (0.15 to 0.6 g.). A solid extract made with 60% alcohol, 1 = 4 of leaves.

**Extractum Cathæ Liquidum.** **Dose.**—1 to 5 minims (0.06 to 0.3 ml.). Strength 2 = 1, prepared with alcohol 60%.

**Guarana** (*B.P.C.*, *P. Helv. V*, *P. Hung.*).

**Dose.**—10 to 60 grains (0.6 to 4 g.) in powder, or infused in a cup of boiling water.

The seeds of *Paullinia Cupana* (Sapindaceæ), roasted and moistened with water, made into a hard paste, rolled into cylinders, and dried. Imported from Brazil. The drug contains 2.5 to 5% of caffeine (guaranine), together with tannin, gum, etc. Is recommended for sick headache and has been employed for its astringent properties in diarrhœa and dysentery. A nerve tonic.

**Elixir Guaranzæ** (*B.P.C.*). **Dose.**— $\frac{1}{2}$  to 2 drachms (2 to 8 ml.). Contains 80% v/v of tincture of guarana flavoured with cinnamon.

**Tinctura Guaranzæ** (*B.P.C.*). **Dose.**—1 to 2 drachms (4 to 8 ml.). 1 in 4.

**Kola** (*B.P.C.*, *P. Helv. V*).

**Dose.**—15 to 45 grains (1 to 3 g.).

Seeds of *Cola vera* (Sterculiaceæ), containing about 1½% of caffeine and traces of theobromine. Tonic and diuretic.

**Fr. Cx.** allows seeds of other varieties of *Cola* providing they contain at least 1.5% caffeine.

**Extractum Kolæ Liquidum** (*B.P.C.*, *Fr. Cx.*).

**Dose.**—10 to 20 minims (0.6 to 1.2 ml.). 1 in 1.

**Elixirium Colæ** (*Fr. Cx.*).

Liquid extract of kola 5%, alcohol (60%) 10%, simple syrup 10%, in a sweet wine.

**[P1] Syrupus Kolæ Compositus (Martindale).**

*Dose.*—1 to 2 drachms (4 to 8 ml.) twice daily.

Iron, quinine and strychnine citrate 3, citric acid 0·3, sodium glycerophosphate 5, liquid extract of kola 50, alcohol 90% 5, syrup of orange to 100. Finished product to be slightly acid. In anorexia, and as a general "tonic."

**Tinctura Kolæ (B.P.C.).**

*Dose.*— $\frac{1}{4}$  to 1 drachm (1 to 4 ml.). 1 in 5. *Fr. Cx.* is similar.

**Vinum Kolæ (Fr. Cx.).** Macerate powdered kola 60, in liqueur wine 1000, for 10 days.

**Vinum Kolæ (Martindale).**

Kola in coarse powder 1, in sherry 25, macerate for 7 days, filter and flavour with essence of vanilla.

**[P1] Revitone (Roche Products, Welwyn Garden City).** Contains per oz. "Ext. Kola glycerin sacch." (= Sem. Kolæ 88 gr.), "Arsylen" brand of sodium allylarsenate 0·088 gr., dried extract of nux vomica 0·28 gr., sodium acid phosphate 16·22 gr., manganese chloride 0·09 gr. *Dose.*—1 or 2 teaspoonfuls 3 times daily. General tonic.

**Vitabene Brand Tablets (Eno, London).** Tablets each weighing about  $7\frac{1}{2}$  gr. and containing tricalcium phosphate 30·9, stabilised kola powder 26·0, potassium carbonate 14·0, anhydrous sodium carbonate 14·0, magnesium carbonate 3·2, caffeine alkaloid 1·6, manganese carbonate 3·2, cupric sulphate 0·1, orange flavouring powder 0·6, excipient 8·4. Advocated in convalescence, etc. *Dose.*—For adults, 2 tablets thrice daily after meals; children, 1 tablet.

**Maté. Syn. and Prop. Name.** YERBA, PARAGUAY TEA, JESUIT TEA, HERVEA (*H. J. Lee, London*). The dried leaves of *Ilex paraguayensis* (Ilicaceæ). Contain 0·2 to 2% of caffeine. It is less astringent than tea and as a beverage has no disagreeable after-effects.

More than 18,000,000 people in S. America drink maté. Thought to ward off rheumatism, and produces exhilarating yet soothing effect on nerves and has very sustaining properties. Principal beverage of rural working classes in the Argentine, Paraguay and Brazil.—*J. trop. Med. (Hyg.)*, 1925, 320.

**CALCIFEROL**

(with VITAMIN A)

*B.P. Add. I.*

$C_{28}H_{43}OH = 396\cdot3$ .

**Syn. and Prop. Name.** VITAMINA D (*Fr. Cx.*), VIOSTEROL, RADIOSTOL (*British Drug Houses, London*).

*Dose.*—Prophylactic (daily) for an infant  $\frac{1}{2400}$  to  $\frac{1}{1200}$  grain (0·025 to 0·05 mg.), approximately equivalent to 1000 to 2000 units. Therapeutic (daily) for an infant  $\frac{1}{1200}$  to  $\frac{1}{600}$  grain (0·05 to 0·075 mg.), approximately equivalent to 2000 to 3000 units.

Calciferol is vitamin D<sub>2</sub>, prepared by the ultra-violet irradiation of ergosterol, and possessing a potency of 40,000 i.u. of anti-rachitic activity per mg. It occurs in colourless, odourless crystals, melting at 115° to 119° *in vacuo*.

**Insoluble** in water, but readily soluble in alcohol 95%, ether, chloroform and acetone; less soluble in vegetable oils.

For full details of the chemistry and assay of calciferol, see Vol. II.



### Vitamin D.

Under the term "vitamin D" are included several substances possessing the property of preventing or curing rickets. These substances are derivatives of sterols which acquire anti-rachitic properties when exposed to ultra-violet light. The two most important are those produced by the irradiation of ergosterol and of 7-dehydrocholesterol.

Ergosterol is present in ergot, some fungi and moulds and in yeast. When irradiated with ultra-violet light of certain wavelengths, it undergoes a series of changes resulting in the formation of calciferol, generally spoken of as vitamin D. The conversion is never quantitative, and even under the best conditions the product contains only about 50% of calciferol. If the irradiation is carried further, especially if the calciferol is dissolved in alcohol, some of the calciferol is decomposed to form a compound which has been termed "substance 248" or toxisterol. Some of the toxic effects reported by the administration of vitamin D in the form of irradiated ergosterol, when this was first used clinically, were undoubtedly due to the presence of this product of over-irradiation. Toxisterol is not formed if the irradiation is conducted with ether as the solvent.

Cholesterol is present in many animal fats and associated with it in the natural state are small quantities of 7-dehydrocholesterol. This substance has been prepared synthetically, and both the natural and the synthetic compounds can be "activated," *i.e.*, rendered anti-rachitic, by ultra-violet light. Activated 7-dehydrocholesterol is the chief form of vitamin D present in fish-liver oils. This substance is termed *vitamin D<sub>3</sub>* to distinguish it from calciferol. The term *vitamin D<sub>1</sub>* was at one time applied to a mixture of lumisterol and calciferol, which was then believed to be the pure vitamin D.

Vitamin D in the form of calciferol, dissolved in olive oil, cod-liver oil, halibut-liver oil or in liquid paraffin is unchanged, or at most only slightly changed, after fifteen to twenty months' storage. The same is true of the natural vitamin D content of both halibut-liver oil and cod-liver oil.

**Hypervitaminosis D.** Although the toxic dose of vitamin D is many times the therapeutic dose, there is evidence that 10,000 to 20,000 units is on the borderline of toxicity and it would appear safer not to exceed a maximum therapeutic dose of 5000 units, reduced to 3000 units for infants under 2 years. A single large dose is not likely to give rise to any permanent ill-effects, but continued overdosage may cause abnormal deposition of calcium in various tissues of the body due to hypercalcaemia. This may lead to the formation of renal calculi, osteoporosis and arteriosclerosis, and there is now no question but that at a certain dosage even pure crystalline vitamin D may prove fatal to man. The symptoms of overdosage are loss of appetite, lassitude, pallor, polyuria, profuse sweating, nausea, vomiting, headache and loss of weight. Elevation of the calcium content of the blood serum

above 12 mg. per cent. is an indication of toxic effect. Even with therapeutic dosage an adequate amount of calcium salts and phosphorus compounds in the diet is essential during the administration of vitamin D.

Different species of animals vary markedly in resistance to excess dosage. Whereas toxic effects in rats only occur after giving several thousand times the therapeutic dose, in dogs 20 times the curative dose causes death. The human subject may share this high susceptibility with the dog and clinical evidence points that way.—*Brit. med. J.*, ii/1931, 352.

A fatal case of hypervitaminosis D in a baby of 11½ months. Young infants may have idiosyncrasy to the vitamin D contained in cod-liver oil as well as to artificially prepared calciferol. The present-day tendency to increase the vitamin D potency of cod-liver oil is undesirable and unnecessary; that to which the public is accustomed, and upon which popular dosage is based—viz., about 100 i.u. per g.—is sufficient for all purposes. There is no reason whatever to administer cod-liver oil to infants during the summer months when diet and hygienic conditions are satisfactory and there is no evidence of rickets.—*L. Thatcher, Lancet*, i/1936, 20.

Irradiated ergosterol given by the mouth in very large doses causes the formation of urinary calculi. It is suggested that this is dependent on an increased absorption of calcium and phosphate from the gut and their excretion by the kidneys.—*W. E. Dixon and J. C. Hoyle, Brit. med. J.*, ii/1928, 883.

When vitamin D is introduced into the food by irradiation this process influences not only the sterols but also each chemical element present in the food thus treated. The complex carbohydrates are hydrolised; the proteins are transformed, their properties becoming changed; the amino-acids are also affected; the fats become viscous and are oxidised; the ferments and vitamins A and C are destroyed. Although accidents of D-hypervitaminosis are less frequent than they were, with our growing experience of these questions we must lay it down that the increasing and uncontrolled use of food (flour, biscuits, butter, chocolate, milk, etc.), the vitamin D content of which has been artificially increased by irradiation, cannot be recommended.—*G. L. Randoin, Quart. Bull. Hlth Org. L.O.N.*, 1936, 493.

While calcium is essentially necessary in pregnancy there seems to be some factor or factors when viosterol is used with it which render it either more assimilable, its retention and deposition more pronounced, or which produce an irregular mobilisation regardless of whether the calcium is given as inorganic adjuncts or by its ingestion in foods. Following the routine use in obstetric cases of 5 drops (0.3 ml.) of viosterol three times a day for 2 weeks, alternated with 5 grains of calcium every day for 2 weeks, calcified areas in the placentas and a decrease in the size of the fontanelles with fusion of the cranial sutures, which could be shown by the roentgenogram before delivery, were noted. This was easily demonstrated after delivery with a consequent lessened moulding of the fetal head and an increase in the length of labour. Marked calcification was found in the kidneys of 3 stillborn infants without any other apparent aetiology. Considerably more research work is advised before the promiscuous use of viosterol is continued, and cod-liver oil seems preferable.—*W. Brehm, per J. Amer. med. Ass.*, ii/1937, 1490.

The death of a man is recorded which was undoubtedly the result of over-dosage of a concentrated solution of activated ergosterol; a doctor administered to himself 2,300,000 units daily for 18 days, i.e., 18,000 units per kilo, or ten times what he had intended to take.—*Brit. med. J.*, i/1937, 1269.

A case of congenital parathyroid deficiency controlled by oral administrations of vitamin D<sub>2</sub> (Calciferol) in oil, 500,000 units weekly. Despite the continued administration of this large dosage for nearly six years no signs of hypervitaminosis D have appeared.—*H. P. Himsworth and M. Maizels, Lancet*, i/1940, 959.

**Uses.** The following summary of "Allowable Claims," drawn up by the Council on Pharmacy and Chemistry of the A.M.A. (N.N.R. 1940), serves as a useful indication of the present position of vitamin D therapy.

Vitamin D is recognised as a specific in the treatment of infantile

rickets, spasmophilia and osteomalacia, diseases which are manifestations of abnormal calcium and phosphorus metabolism. Vitamin D is valuable in the preventive as well as curative treatment of these diseases. Complications such as certain renal diseases or glandular malfunction may preclude normal response to vitamin D therapy. During acute infections, especially of the gastro-intestinal tract, vitamin D may prove ineffective because poorly absorbed. There is clinical evidence to justify the statement that vitamin D plays an important role in tooth formation and maintenance of normal tooth structure, but there is no warrant for the claim that adequate vitamin D intake will ensure normal tooth structure or will prevent dental caries. Animal experimentation has shown that correction of an inadequate intake of vitamin D results in the more economical utilisation of calcium and phosphorus, and also that the undesirable effects of improper ratios of calcium and phosphorus in the diet can largely be overcome by normal intake of vitamin D. The importance of these observations in their application to man is not entirely apparent, but it may be stated that vitamin D has a favourable influence on calcium and phosphorus metabolism. The vitamin D requirement is greatest during the period of infancy. Beyond the age of infancy the exact vitamin D requirement of man under any specified conditions is not known, but it appears that the requirement during pregnancy and lactation is increased. Clinical evidence does not warrant the claim that massive doses of vitamin D are of benefit in chronic arthritis, in allergic disorders, or in psoriasis.

Apart from its use in rickets it is the proper remedy for infantile tetany (which is due directly to hypocalcemia), osteomalacia, coeliac disease (as a safeguard against rickets), and it is essential to nursing and expectant mothers, not so much to protect the young as to improve the calcium assimilation of the mother herself and help her to replace the minerals lost to the child or in her milk.—L. J. Harris, *Brit. med. J.*, ii/1933, 371.

**CARIES.** The influence of vitamin D on the structure of the teeth.—May Mellanby, Pt. I, *Spec. Rep. Ser. med. Res. Coun., Lond.*, No. 140, 1929; Pt. II, *ibid.*, No. 153, 1930; Interim Report on "The Influence of Diet on Caries in Children's Teeth," *ibid.*, No. 159, 1931; Pt. III, *ibid.*, No. 191, 1934; *Brit. med. J.*, i/1932, 507; ii/1932, 749.

Vitamin D deficiency, dental caries, and tonsillar enlargement. A clinical investigation of some late effects of rickets.—H. M. M. Mackay, *Lancet*, i/1931, 1230.

The influence of diet on caries in children's teeth.—Final Report of the Committee for the Investigation of Dental Disease, *Spec. Rep. Ser. med. Res. Coun., Lond.*, No. 211, 1936.

**DERMATITIS.** Good results in the treatment of dermatitis from a wide variety of causes by injection of vitamins, intramuscular injections of 2 ml. of an oily solution of vitamins A and D at a concentration of 10,000 i.u. per ml. being given three times weekly, with, in some cases an external application of an oil solution of vitamin D. This treatment not only cured the dermatitis in nearly every case but also seemed to convey immunity.—Dainow, per *Mfg Chem.*, 1940, 213.

**ECZEMA.** In a group of eczema cases of both endogenous and exogenous origin, it was shown that the administration, in large doses, of vitamin D and a mixture of vitamins A and D proved useful in the great majority of cases. It accelerated the recovery, and the results were equally good in cases of internal and external origin. The treatment was more efficacious in young subjects and where there was an absence of endocrine disturbances.—M. Cornel, per *Brit. J. Derm.*, 1935, 47, 490.

**OSTEOMALACIA** which occurred in field workers in India, in spite of their being exposed to strong sunlight, yielded to the administration of 4 drachms of sun-irradiated dried brewers' yeast daily for 4 weeks.—D. C. Wilson, *Lancet*, i/1932, 1142.

**RICKETS.** The dose of pure concentrated vitamin D<sub>2</sub> required for the complete cure of florid rickets is 12 to 15 mg. given in a single dose, which corresponds almost exactly with the total amount given in the ordinary therapeutic course comprising daily dosage for 2 to 3 months.—H. U. Kottgen, per *Brit. med. J. Epit.*, i/1938, 58.

The number of units required for the prevention of rickets lies between 500 and 1500 daily, the daily requirement varying with age, rate of growth, presence or absence of infection, and the diet of the child. During the first few years 1000 to 1500 units should be given daily, and this should be continued right through the summer.—C. Asher, *Practitioner*, ii/1940, 61.

The course of healing in 12 infants and children with active rickets was studied, 6 being given vitamin D<sub>2</sub> and 6 vitamin D<sub>3</sub> in amounts equivalent to 2000 i.u. daily. The results revealed no significant difference between the therapeutic effects of these two vitamins.—N. Morris and M. M. Stevenson, *Lancet*, ii/1939, 876.

The therapeutic effects of pure specimens of vitamin D<sub>2</sub> from irradiated ergosterol and of vitamin D<sub>3</sub> from irradiated 7-dehydrocholesterol were compared in 13 pairs of patients with osteomalacia, and in two pairs with late rickets, among Indians aged 6 to 70 in the Punjab. The results showed the two preparations to be equally effective, a dose of 21,000 i.u. causing improvement in a week.—D. C. Wilson, *Lancet*, i/1940, 961.

**Emulsio Calciferolis (I.H.). Syn. D EMULSION.**

Solution of calciferol 5 m., arachis oil 10 m., chloroform  $\frac{1}{10}$  m., benzoic acid  $\frac{1}{10}$  gr., vanillin  $\frac{1}{10}$  gr., mucilage of acacia 10 m., water to 1 dr. For a child of one year.

**Ergosterol Activatum in Oleo (U.S.P. XI Supp. II). Syn. LIQUOR ERGOSTEROLIS IRRADIATI, VIOSTEROL IN OIL.**

*Average dose.*—5 minims (0.3 ml.).

A solution of activated ergosterol in an edible vegetable oil, containing not less than 10,000 units of vitamin D per g.

**Liquor Calciferolis (B.P. Add. I).**

*Dose.*—Prophylactic (daily) for an infant, 5 to 10 minims (0.3 to 0.6 ml.), approximately equivalent to 1000 to 2000 i.u. Therapeutic (daily) for an infant, 10 to 15 minims (0.6 to 1 ml.), approximately equivalent to 2000 to 3000 i.u.

A solution of calciferol in a suitable oil, such as arachis oil, containing 3000 i.u. per gramme. It replaces irradiated solution of ergosterol B.P., which was permitted to contain other products of the irradiation, together with unchanged ergosterol, in addition to calciferol.

**Liquor Vitamini D Concentratus (B.P. Add. II).**

*Dose.*— $\frac{1}{2}$  to 3 minims (0.03 to 0.2 ml.), approximately equivalent to 250 to 1500 units of vitamin D.

A solution of vitamin D containing 10,000 i.u. per gramme. It consists either of fish-liver oils or of a solution of a source of vitamin D in a vegetable oil such as arachis oil.

**Solutum Vitamine D cum Oleo (Fr. Cx.)** contains the equivalent of 10,000 units of vitamin D per ml. in olive oil.

**Tab. Calc. c. Vit. D (N.I.F.).** Each tablet contains calciferol  $\frac{1}{1000}$  gr., calcium sodium lactate  $7\frac{1}{2}$  gr., calcium phosphate  $2\frac{1}{2}$  gr. Vitamin D content 500 units.

**Calcium c. Vitamin D (Crookes Laboratories, London).** Liquid for injection in 1 ml. ampoules, each containing calcium 1 in 2000, vitamin D 5000 i.u. Also as liquid for oral use, 1 drachm containing calcium 1 in 2000, vitamin D 250 i.u., and as capsules, containing the equivalent of 1 drachm of liquid.

**Calcivitan** (*Richter, London*). Tablets contain calcium gluconate  $7\frac{1}{2}$  gr. with vitamin D 800 i.u. *Dose*.—1 or more tablets daily before meals. During pregnancy and lactation and wherever calcium is indicated.

**Calcydic** (*Allen & Hanburys, London*). Chocolate-flavoured granules containing per dr.  $7\frac{1}{2}$  gr. of dicalcium phosphate, 1500 i.u. of vitamin D, and 30 gr. of dextrose. *Dose*.— $\frac{1}{2}$  to 2 drachms.

**Calfo-Rayol Capsules** (*Squibb, New York; Savory & Moore, London*). Contain  $4\frac{1}{2}$  gr. dicalcium phosphate, 3 gr. calcium gluconate and 330 i.u. vitamin D.

**Calsimil** (*British Drug Houses, London*). Tablets containing 5 gr. of calcium sodium lactate and 500 i.u. of vitamin D.

**Calsolact D** (*Allen & Hanburys, London*). Tablets containing  $7\frac{1}{2}$  gr. of calcium sodium lactate with 1000 units of vitamin D.

**Davitamon D** (*Organon Laboratories, London*). Solution and 1 ml. ampoules containing 5000 i.u. of vitamin D per ml. **Davitamon D Forte** contains 12,500 i.u. per ml.

**Decufer** (*Organon Laboratories, London*). Uncoated tablets each containing vitamin D 500 i.u., iron 20 mg., and copper 0.2 mg.

**Ostelin Preparations** (*Glaxo Laboratories, London*). **LIQUID**. A glycerin suspension of calciferol containing 5000 i.u. of vitamin D per ml. **TABLETS**. Calcium glycerophosphate 2 gr., with 500 i.u. of vitamin D. **EMULSION**. 3000 i.u. of vitamin D per oz. **Colloidal Calcium with Ostelin**. A preparation of vitamin D for injection containing per ml. 5000 i.u. of vitamin D and 0.5 mg. of colloidal calcium. For urticaria, angioneurotic oedema, chilblains and other allergic states, also for delayed union of fractures. *Dose*.—1 ampoule (1 ml.) at 3-day intervals, or daily for delayed union. **High Potency Ostelin Tablets** contain 50,000 i.u. of vitamin D. *Dose*.—1 to 6 daily, or more. Parathyroid tetany, chronic arthritis, rickets, hay-fever, etc.

**Ostocalcium** (*Glaxo Laboratories, London*). Tablets contain  $7\frac{1}{2}$  grains of calcium sodium lactate,  $2\frac{1}{2}$  grains of calcium phosphate and 500 i.u. of calciferol. *Dose*.—1 to 12 tablets daily.

**Radiostol Solution** (*British Drug Houses, London*). A brand of Liquor Calciferolii. **Radiostol Pellets** contain calciferol equivalent to 3000 i.u. in each. A solution in liquid paraffin for external application in the treatment of wounds, etc., is also available.

**Viozin** (*Glaxo Laboratories, London*). An ointment of calciferol (500 i.u. per g.) with zinc oxide in a wool fat and paraffin base. Promotes healing of wounds and varicose ulcers.

**Dihydrotachysterol**. *Syn.* A.T.10 (*Merck, Darmstadt; Savory & Moore, London*).

An oil-soluble fraction of irradiated ergosterol (isolated by Holtz and Windaus), which does not contain vitamin D but has a specific effect on the calcium content of the serum. Taken by the mouth it causes hypercalcaemia in animals and men, and is employed in the treatment of post-operative tetany and parathyroid insufficiency. Dosage is controlled by estimation of the blood calcium.

No other preparation gives such excellent results in the treatment of parathyroid tetany, but it is a very potent preparation and should not be used indiscriminately. Excessive doses have been shown to result in decalcification of bone of experimental animals and greatly increased urinary calcium, metastatic calcification, severe gastro-intestinal upsets, and bleeding from the bowel. It seems advisable to give small doses of calcium simultaneously, and frequent determination of serum calcium is necessary. Of four patients (all unsuccessfully treated for years by other methods) treated by dihydrotachysterol two have had approximately normal blood calcium and no symptoms for 9 months and the other two for 3 months each. The drug must be continued in small maintenance doses to keep the blood calcium at normal level. The dose ranges from 0.25 to 0.75 ml. daily, with a calcium intake ranging from 2 to 10 g. of calcium lactate or gluconate. There seems no necessity to order severe restriction of the

phosphorus intake. The cumulative effect of the drug is important; it exerts its action over a period of days or weeks and takes several days for any marked effect to appear.—C. M. MacBryde, *J. Amer. med. Ass.*, i/1938, 767.

Dihydrotachysterol has certain very definite advantages over parathyroid extract in the treatment of chronic tetany; (1) the effect is more prolonged, (2) it is taken orally, (3) no tolerance is developed, (4) it is less expensive, (5) it is stable and retains its potency when kept at ordinary room temperature. Six women suffering with chronic hypoparathyroidism following thyroidectomy and one with idiopathic tetany were completely relieved by treatment with dihydrotachysterol. The previous duration of the symptoms of tetany ranged from 3½ to 17 years, and all previous therapy had been comparatively ineffective except for temporary relief afforded by injections of parathyroid extract and calcium.—C. M. MacBryde, *J. Amer. med. Ass.*, ii/1938, 304.

A.T.10 was effective in controlling the parathyroid deficiency in a case of congenital parathyroid deficiency, but appeared less reliable in its action than vitamin D<sub>2</sub>.—H. P. Himsworth and M. Maizels, *Lancet*, i/1940, 959.

#### Vitamin A. $C_{40}H_{56}O$ = 286.44.

Vitamin A has been isolated from the unsaponifiable fraction of fish-liver oils in the form of pale yellow crystals. In structure it is closely related to the plant pigment carotene which exists in three isomeric forms all of which are converted to some extent into vitamin A in the livers of man and animals. Of the three isomers, the *beta* compound is considered to be the most active, and it is probable that the molecule of *beta*-carotene undergoes hydrolysis with the formation of two molecules of vitamin A. *Alpha* and *gamma* carotenes each yield only one molecule of vitamin A for one molecule of carotene and have only half the vitamin A activity of the *beta* compound. Carotene is a dark yellow or orange, crystalline substance, nearly tasteless and possessing a slight aromatic odour; almost insoluble in water, slightly soluble in alcohol, more soluble in ether, light petroleum, fats and oils, and freely soluble in chloroform and benzene. Carotene occurs in blood in colloidal combination with albumin; it exists in the spleen, liver, bone marrow, retina of the eye, corpus luteum, kidneys and subcutaneous fat. The vitamin A of plants is due to the presence of *alpha*, *beta* and *gamma* carotenes and to kryptoxanthine; that of animal tissues is due to both vitamin A and carotene, while fish-liver oils contain vitamin A but no carotene.

Vitamin A and its precursors are stable to heat in the absence of oxidising agents, and the ordinary cooking processes do not destroy the vitamin A activity of vegetables. Frozen foods retain their vitamin A content over long periods of storage, but rancid fats have a catalytic effect on vitamin A destruction. Light also accelerates the destruction of vitamin A, hence cod-liver oil and other fish-liver oils should be stored in bottles of amber-coloured glass.

For full details of the chemistry and assay of vitamin A see Vol. II.

**Human Requirements.** The exact daily requirement of vitamin A by human beings has not been determined, but an optimal intake of from 3000 to 5000 i.u. daily has been recommended for healthy adults, and from 6000 to 8000 i.u. daily for

pregnant and nursing women. No toxic effects have been recorded from excessive dosage.

The vitamin A requirement of the human adult has been assessed at 2500 to 3000 i.u. per day of preformed vitamin, or some 5000 i.u. of carotene in oily solution. If the daily intake of vitamin A in milk and vitaminised margarine is assessed at about 1000 i.u., then the equivalent of some 1500 i.u. of preformed vitamin must be made up by vegetables. Of these, the carrot is the most valuable, a mature carrot containing an average of 200 i.u. of carotene per g. On this basis about 2 oz. of carrots would be needed to make up the daily requirement in the absence of other vegetables. Assuming other green vegetables to supply half the total requirement over the year, an allowance of about 1 oz. of carrots per day should meet the normal requirements.—*Nature, Lond.*, i/1941, 132.

**Dark-Adaptation Test.** Since it is known that vision at low illumination is dependent on the presence of visual purple in the retina and the content of this pigment in the retina is decreased in avitaminosis A, and since night-blindness is an early symptom of vitamin A deficiency, an examination of the ability of the eyes to adapt themselves to vision in light of low intensity is employed to ascertain the presence of incipient vitamin A deficiency. For this purpose the Birch-Hirschfeld photometer is usually employed, by means of which it is possible to measure the sensitivity to light of the eyes following partial dark-adaptation.

Dark-adaptation as an index of adequate vitamin A intake. Technique and preliminary results.—J. R. Mutch and H. D. Griffith, *Brit. med. J.*, ii/1937, 565.

Among poor-class children attending elementary schools in London and Cambridge, examined by the dark-adaptation test, roughly 40 to 50% of the total were normal, 20 to 30% slightly below normal and a further 20 to 30% were definitely deficient. Among 30 better-fed boys at a public school none were definitely deficient and only 3 were "border line." Children found sub-normal returned slowly to normal after treatment with large amounts of vitamin A, whereas an equal number of controls left untreated remained sub-normal. The test is only capable of detecting deficiency and not of assessing different levels of normality. Deficiency seems less common among adults than in children.—L. J. Harris and M. A. Abbasy, *Lancet*, ii/1939, 1355.

**Uses.** The following summary of "Allowable Claims," drawn up by the Council on Pharmacy and Chemistry of the A.M.A. (*N.N.R.*, 1940), serves as a useful indication of the present position of vitamin A therapy.

Vitamin A is specific for nyctalopia, or night-blindness due to vitamin A deficiency, but not when the condition is due to congenital defects or to diseases other than avitaminosis A. The claim that the administration of vitamin A to drivers of motor-cars will diminish the chance of accidents from driving at night is not accepted.

Vitamin A is reported to be effective in the treatment of certain types of hyperkeratosis of the skin of persons suffering from severe deficiency of vitamin A.

Present indications are that vitamin A is an aid towards establishing the resistance of the body to infections in general only when there has been an exhaustion of body reserves of the vitamin and the ingestion of vitamin A is inadequate. It has not been shown to be specific in the prevention of colds, influenza and such infections, nor has it been demonstrated that ingestion of vitamin A far in excess of that necessary for normal body function, and readily obtained from a properly selected diet, is an aid in preventing

various types of infections. A deficiency of vitamin A results in a retardation of growth when body stores of the vitamin have been depleted, but it must be borne in mind that vitamin A is not more important in promoting growth than other food essentials. There is at the present time inadequate evidence to warrant the claim that the ingestion of sufficient vitamin A will prevent the formation of renal calculi in man, or that it is useful in the treatment of hyperthyroidism, anaemia, degenerative conditions of the nervous system, sunburn, or ulcerative conditions of the skin.

Is not a general anti-infective agent; it is anti-infective only in a limited way and vitamin A therapy has failed to have any effect as a prophylactic in respiratory diseases, in the common cold in infants, on the incidence of common infections generally, or in treatment of pneumonia. The local infections to which vitamin A deficiency gives rise are of quite a special type, being caused by structural breakdown of membranes; there is no change in the general immunity.—L. J. Harris, *Brit. med. J.*, ii, 1933, 231.

An experiment consisting in the administration over a period of 6 months of a concentrate of vitamins A and D, in daily doses equivalent in vitamin A to rather more than 1 oz. of high-grade cod-liver oil, to 294 poor schoolchildren of Peterhead, with 281 contemporaries acting as controls, showed the rate of growth of the treated children as only slightly better than that of the controls and susceptibility to infection and resistance to established disease were apparently unaffected. The results compared unfavourably with milk experiments. Evidence suggested that the cause of the failure was that the vitamin supplements made good only one dietary deficiency and left uncorrected associated deficiencies of equally essential constituents of the diet. The public must be educated that vitamin supplements do not constitute a short cut to health, but that a well-balanced diet is essential.—R. Sutherland, *Brit. med. J.*, i, 1934, 791.

Perfectly calcified and regularly arranged teeth can be produced by including in the maternal diet during pregnancy and lactation, and in the diet of the offspring at the time of dental development, substances containing much fat-soluble vitamin, calcium and phosphorus. Cereals, especially oatmeal, tend to produce badly developed (hypoplastic) teeth and call for a correspondingly larger supply of calcifying foods. The teeth of the majority of children in the British Isles are imperfect in structure and have a roughish surface: dental caries is more likely to attack such teeth than perfect teeth with normal enamel and dentine and a comparatively smooth surface. The resistance of teeth to caries can be increased independently of their original structure by giving a diet of high calcifying activity, while resistance is decreased by a diet rich in cereals and of low calcifying properties. Deficiency of vitamin A or carotene plays an important part in development of periodontal tissues and control of onset of periodontal disease, including pyorrhoea.—May Mellanby, *Spec. Rep. Ser. med. Res. Coun., Lond.*, No. 191, 1934; *Brit. med. J.*, i, 1934, 252.

### Liquor Vitamini A Concentratus (B.P. Add. II).

**Dose.**—1 to 5 minims (0.06 to 0.3 ml.), approximately equivalent to 2500 to 12,500 i.u. of vitamin A.

A solution of vitamin A possessing 50,000 units of vitamin A activity per g., and consisting of fish-liver oils or of a solution of a source of vitamin A in a vegetable oil such as arachis oil.

Vitamin A is of value as a local application in certain ophthalmic conditions, in particular in the herpetic forms of corneal disease and other corneal lesions and in injuries and burns of the conjunctiva. Because of its analgesic and lubricating effect it is invaluable for injuries from gases used in industry and warfare. It not only helps epithelialisation, but is a protective agent for the epithelium.—*Brit. med. J.*, i, 1940, 354.

### Liquor Vitaminae-A (B.P.C.).

**Dose.**—5000 to 50,000 units.

A solution in arachis or other suitable vegetable oil of a concentrate of mammalian or other livers. It contains 60,000 units of vitamin A per g.; a small amount of vitamin D may also be present.



**Vitamina A Naturalis in Oleo (U.S.P. XI Supp. II).***Average daily dose.*—5 minims (0.3 ml.).

A solution of vitamin A containing 50,000 to 60,000 units of vitamin A and not more than 1000 units of vitamin D per gramme. It consists of either fish-liver oil, plain or diluted with a vegetable oil, or of a solution of a vitamin A concentrate obtained from animal sources, in fish-liver oil or vegetable oil.

**Avoleum (British Drug Houses, London).** A concentrated preparation of vitamin A, without admixture of vitamin D, containing 30,000 i.u. per g. In liquid or capsules containing 3 m. *Dose.*—3 to 9 minims daily.

**Davitamon A (Organon Laboratories, London).** Solution of vitamin A containing 6000 i.u. per ml. **Davitamon A Forte** contains 60,000 i.u. per ml., and is also issued in 1 ml. ampoules for injection.

**Essogen (Trufood, London).** A vitamin A preparation with a blue value of 2000. Supplied in capsules of 2 m.

**Eubion (Evans, Sons, Lescher & Webb, Liverpool).** Chocolate tablets containing vitamin A equivalent to one tablespoonful of best cod-liver oil.

**Planavit A (Pharmaceutical Specialities (May & Baker) Ltd., London).** Standardised solution of vitamin A, prepared from fish-liver oils and containing 25,000 i.u. per ml.

**Prepalin (Glaxo Laboratories, London).** A vitamin A concentrate. Each ml. contains 72,000 i.u. and each 3-minim capsule 24,000 i.u.

**Vulnovitan (Richter, London).** Vitamin A dressing for wounds. Ointment contains 1000 i.u. per gramme; oil contains 2000 i.u. per ml.

**Liquor Vitaminorum A et D Concentratus (B.P. Add. II).**

*Dose.*—1 to 5 minims (0.06 to 0.3 ml.), approximately equivalent to 2500 to 12,500 i.u. of vitamin A and 250 to 1250 i.u. of vitamin D.

A solution of vitamin A 50,000 i.u. and vitamin D 5000 i.u. per gramme. It consists of either fish-liver oils or of a solution of sources of vitamins A and D in vegetable oil such as arachis oil.

**Oleum Vitaminatum (B.P. Add. II).**

*Dose.*—Prophylactic, 15 to 30 minims (1 to 2 ml.), approximately equivalent to 1000 to 2000 i.u. of vitamin A and 100 to 200 i.u. of vitamin D. Therapeutic, 45 to 90 minims (3 to 6 ml.), approximately equivalent to 3000 to 6000 i.u. of vitamin A and 300 to 600 i.u. of vitamin D.

A solution of vitamin A 1000 i.u. and vitamin D 100 i.u. per gramme. It consists of either fish-liver oil or of a solution of sources of vitamins A and D in a vegetable oil such as arachis oil.

**Emulsio Olei Vitaminati (B.P. Add. II).**

*Dose.*—30 to 60 minims (2 to 4 ml.), approximately equivalent to 1000 to 2000 i.u. of vitamin A and 100 to 200 i.u. of vitamin D.

Vitaminised oil 50% v/v. An efficient substitute for emulsion of cod-liver oil.

**Vitaminæ A et D Naturales in Oleo (U.S.P. XI Supp. II).***Average daily dose.*—5 minims (0.3 ml.).

A solution of vitamin A 50,000 to 65,000 units and vitamin D 10,000 to 13,000 units per gramme. It consists of either fish-liver oil, plain or diluted with vegetable oil, or of a solution of a vitamin A concentrate obtained from animal sources in fish-liver oil or vegetable oil.

**Vitamins A and D in Oil for Animal Feeding Purposes (B.S.S. No. 909-1940)** consists of a mixture of vitamins A and D with a suitable marine or vegetable oil, and contains not less than 1000 i.u. of vitamin A and 100 i.u. of vitamin D per g. It must be described as unsuitable for poultry feeding unless the amount of vitamin D declared is fully effective for poultry when tested by the Chick Test.

## POLYVITAMIN PREPARATIONS

**A.B.D. Capsules** (*Abbott Laboratories, London*). Contains vitamins A, B<sub>1</sub>, B<sub>2</sub>, and D. Each capsule is equivalent to 3 dr. of cod-liver oil (*U.S.P.*), 15 oz. of milk in B<sub>1</sub> potency and 2 oz. of milk in B<sub>2</sub> potency.

**A.B.D.G. Capsules** (*Squibb, New York; Savory & Moore, London*). Each capsule contains vitamin A 6600 i.u., B<sub>1</sub> 33 i.u., B<sub>2</sub> 22 microgrammes of riboflavin and D 1320 i.u. *Dose*.—1 to 3 daily.

**Abidon** (*Parke, Davis, London*). Capsules, each containing vitamins A and D equivalent to three drachms of cod-liver oil, vitamin B<sub>1</sub> equivalent to 10 oz. of milk, and vitamin B<sub>2</sub>. **Abidon with Vitamin C**. Capsules, each representing vitamin A 6200 i.u., B<sub>1</sub> 50 i.u., B<sub>2</sub> 20 Sherman units, C 200 i.u. and D 900 i.u.

**Adexolin** (*Glaxo Laboratories, London*). Each 3 m. capsule contains 6000 i.u. of vitamin A and 1000 i.u. of vitamin D, equivalent to 10 ml. of cod-liver oil. Also as emulsion containing 18,000 i.u. of vitamin A and 3000 i.u. of vitamin D per oz.

**Calvitone** (*Martindale, London*). Contains per oz. calcium acid phosphate 5 gr., iron and copper citrate 10 gr., sodium and manganese glycerophosphate 5 gr., vitamin A 16,000 units and vitamin D 800 units. *Dose*.—2 teaspoonfuls repeated. General tonic.

**Davitamon AD** (*Organon Laboratories, London*). Liquid preparation containing vitamin A 6000 i.u., and vitamin D 5000 i.u. per ml. **Davitamon AD Cornfits** are spherical, red, sugar-coated tablets each containing vitamin A 1500 i.u., and vitamin D 1000 i.u. **Davitamon 5**. Sugar-coated tablets each containing vitamin A 1000 i.u., vitamin B 50 i.u., vitamin C 10 mg., vitamin D 200 i.u., P-P factor 0.5 mg.

**Dekadexolin** (*Glaxo Laboratories, London*). A concentrate of vitamins A and D for intramuscular injection. Each ml. contains 60,000 i.u. of vitamin A and 10,000 of vitamin D in oily solution. *Dose*.—1 ml. daily intramuscularly every other day or at longer intervals. Local and general infections, pyrexia, sloughing bedsores, etc.

**F.C.V.D.** (*Crookes Laboratories, London*). Each teaspoonful contains 250 i.u. of vitamin D, 1 mg. of colloidal iron,  $\frac{1}{16}$  mg. of colloidal copper, with orange juice and malt extract. For use in all forms of debility. *Dose*.— $\frac{1}{4}$  to 2 teaspoonfuls three times daily.

**Greenosan** (*Bencard, London*). (Known as Spinatin in Denmark.) Vegetable extracts in tablet form, each 0.3 g. tablet containing chlorophyll 0.003 g. organic iron 0.01 g., lecithin 0.003 g., iodine (combined) 0.005%, with Ca, Mn, Mg, Cu and K in natural organic combination, vitamin A 33 i.u., vitamin C about 27 i.u., and vitamins B<sub>1</sub>, B<sub>2</sub>, D and E. For all conditions due to hypovitaminosis. Stated to be markedly more effective than equal dosage of the vitamins given alone.

**Halcova** (*Crookes Laboratories, London*). A preparation of malt, milk, eggs and chocolate with vitamins A and D.

**Halisterin** (*Richter, London*). Capsules each containing vitamin A 2500 i.u., and vitamin D 1250 i.u. *Dose*.—One thrice daily.

**Hepicoleum** (*Lilly, London*). Capsules ("globules") each containing 8500 i.u. of vitamin A and 1700 i.u. of vitamin D. **Hepicoleum Compound Globules** contain in each not less than 6200 i.u. of vitamin A, 900 i.u. of vitamin D, 200 i.u. vitamin C (10 mg. ascorbic acid), 50 i.u. of vitamin B<sub>1</sub> and 10 Sherman units of vitamin B<sub>2</sub>.

**Irradex** (*Parke, Davis, London*). Liver oil containing vitamins A and D, vitamin B extract, iron and ammonium citrate, and manganese citrate in malt extract base. *Dose*.— $\frac{1}{4}$  to 4 teaspoonfuls. Malnutrition and debility.

**Multivite** (*British Drug Houses, London*). Chocolate-coated pellets containing in standardised amounts vitamins A, B, C, and D.

**Nestrovite** (*Roche Products, Welwyn Garden City*). Preparations containing vitamins A, B<sub>1</sub>, C and D, available as an emulsion or in tablets. The emulsion contains per teaspoonful 5000 i.u. of vitamin A, 83.5 i.u. of vitamin B<sub>1</sub>, 300 i.u. of vitamin C, and 500 i.u. of vitamin D. The tablets each contain 5000 i.u. of vitamin A, 166 i.u. of vitamin B<sub>1</sub>, 400 i.u. of vitamin C and 500 i.u. of vitamin D. *Dose*.—Infants, 1 teaspoonful of emulsion daily; older infants, increase to  $\frac{1}{4}$  to 2 teaspoonfuls, or 1 tablet, daily; children and adults, 3 teaspoonfuls of emulsion, or 2 tablets daily.

**Parivitan** (*Richter, London*). Syrup containing per fl. oz. vitamin A 15,000 i.u., vitamin D 3000 i.u., organically combined iron 14 gr., calcium, sodium and potassium hypophosphites, of each  $2\frac{1}{2}$  gr., with manganese and copper of each  $\frac{1}{2}$  gr., in a syrup of liquid glucose base. *Dose*.—2 teaspoonfuls 2 to 3 times daily.

**Penta-Kaps** (*Abbott Laboratories, London*). Capsules each containing 6200 i.u. of vitamin A, 900 i.u. of vitamin D, 75 i.u. of vitamin B<sub>1</sub>, 20 Sherman units of vitamin B<sub>2</sub> and 200 i.u. of vitamin C.

**Polyvitamin Co.** (*Hewlett, London*). Emulsion contains vitamins A, B, C and D. Oil contains A, D and E. Capsules, 5 m., also contain an oily solution of A, D and E.

**Priovit** (*Bayer Products, London*). Pellets containing vitamin B<sub>1</sub> 0.5 mg.; vitamin B<sub>2</sub> 0.25 mg.; vitamin C 25.0 mg.; factor P (citrin) 5.0 mg. Advocated for conditions associated with increased metabolism, e.g., febrile diseases, endocrine disorders, hypovitaminosis during pregnancy and lactation.

**Radiostoleum** (*British Drug Houses, London*). Preparations of vitamins A and D. Liquid contains per g. 15,000 i.u. of vitamin A and 3000 i.u. of vitamin D. Capsules 3 m. contain the equivalent of 6 m. of the liquid. A 10% emulsion is also available for administration to infants. **Concentrated Radiostoleum for Injection** contains 75,000 i.u. of vitamin A and 15,000 of vitamin D in each g., and is used in ampoules of 1 ml. for intramuscular injection.

**Rayolex Tablets** (*Squibb, New York; Savory & Moore, London*). Tablets contain 3300 i.u. vitamin A and 660 i.u. vitamin D.

**Syrup Minadex** (*Glaxo Laboratories, London*). Each fl. oz. contains vitamin A 18,000 i.u., vitamin D (calciferol) 3000 i.u., iron and ammonium citrate  $13\frac{1}{2}$  gr., calcium glycerophosphate 2 gr., potassium glycerophosphate  $\frac{1}{2}$  gr., sodium glycerophosphate  $\frac{1}{2}$  gr., manganese glycerophosphate  $\frac{1}{2}$  gr., copper sulphate  $\frac{1}{2}$  gr. *Dose*.— $\frac{1}{2}$  to 2 teaspoonfuls thrice daily.

**Vitapex** (*Paines & Byrne, London*). Vitamin A in oil, available as liquid (35,000 i.u. per g.) or capsules each containing 3500 i.u.

**Vitmar** (*Vitmar, London*). *Dose*.—An egg-spoonful after meals every day. Described as a food containing vitamins A, B, and C, suitable for backward and delicate children. It is stated to have a food value of 400 calories per 100 g.

## CALCIUM

Ca = 40.08

**Calcii Carbonas** (*B.P., U.S.P. XI, Fr. Cx., P. Helv. V, etc.*).  $\text{CaCO}_3 = 100.08$ . *Syn.* CALCII CARBONAS PRÆCIPITATUS, PRÆCIPITATED CALCIUM CARBONATE, PRECIPITATED CHALK, CRAIE PRÉPARÉE, GEFÄLLTES CALCIUM CARBONAT.

*Dose*.—15 to 60 grains (1 to 4 g.).

White insoluble powder.

*Uses*. Much employed in diarrhoea and dysentery and as an ingredient in tooth powders. A valuable antacid in gastric hyperacidity and in gastric and duodenal ulcer.

Diarrhoea of gastric origin is well treated by calcium carbonate and calcium phosphate equal parts, a teaspoonful thrice daily.

Its chief use in ulcer treatment is to relieve pain and heartburn, and for this purpose should be given in doses of from 60 to 90 gr. If the gastric acidity is known to be exceptionally high a big dose may be given at bedtime or more often. The constipation which it causes may be met by increasing the dose of magnesia.—T. L. Hardy, *Practitioner*, 1/1937, 436.

**Creta** (*B.P., U.S.P. XI*). *Syn.* CRETA PRÆPARATA.

*Dose*.— $\frac{1}{2}$  to 1 drachm (1 to 4 g.).

A native calcium carbonate purified by elutriation. Consists of the tests of cretaceous foraminifera such as *Globigerina* and

*Textularia*, together with minute rounded bodies (morpholites), and contains when dried not less than 97% of  $\text{CaCO}_3$ .

**Insoluble** in water or alcohol.

**Blair's Tooth Powder.** Dissolve 3 of soap in about 4 of water, mix intimately with about 25 of precipitated chalk and dry at moderate heat. Dissolve catechu 1 in alcohol 5 and mix intimately with precipitated chalk 25. Mix equal parts of oil of wintergreen and oil of sassafras with a further 25 of precipitated chalk, using 6 drops of mixed oils for each 100 g. of powder. Mix the three portions and sift.

**Creta cum Camphora (B.P.C.).** *Syn.* CAMPHORATED CHALK. Camphor 10%, in calcium carbonate. It loses camphor readily and should be stored in well-closed containers; the freshly prepared mixture may contain less than 10% of camphor.

**Mistura Cretæ (B.P.C.).** Chalk Mixture.

*Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.).

Contains 3% with sugar 6% and a little tragacanth, in cinnamon water. The powders are generally kept mixed in a dry condition, and cinnamon water added as required.

**Mistura Cretæ (U.S.P. XI).**

*Average dose.*— $\frac{1}{2}$  ounce (15 ml.).

Compound chalk powder 20, cinnamon water 40, in water to 100.

[P1] **Mist. Cret. c. Opio (N.I.F.).** Chalk 40 gr., compound powder of tragacanth 5 gr., tincture of opium 5 m., chloroform water to  $\frac{1}{2}$  oz.

[P1] **Mist. Cret. Aromat. c. Opio (N.I.F.).**

Aromatic powder of chalk 20 gr., compound powder of tragacanth 5 gr., tincture of catechu 10 m., tincture of opium 5 m., chloroform water to  $\frac{1}{2}$  oz.

[P1] **Mistura Cretæ Composita (B.P.C.).**

*Dose.*—For adults, 1 ounce (30 ml.); for a 12 year old child,  $\frac{1}{2}$  ounce (15 ml.); for a 7 year old child, 2 drachms (8 ml.).

1 oz. contains 9 gr. of aromatic powder of chalk, 9 gr. of chalk,  $\frac{1}{2}$  dr. of tincture of catechu and 3 m. of tincture of opium.

Closely resembles the mixture formerly known as Board of Health Cholera Mixture.

**Pulvis Cretæ Aromaticus (B.P.).**

*Dose.*—10 to 60 grains (0.6 to 4 g.).

Contains 25% of chalk, with cinnamon, nutmeg, clove, cardamom and sucrose.

**Pulvis Cretæ Compositus (U.S.P. XI).**

*Average dose.*—30 grains (2 g.).

Prepared chalk 30, acacia 20, sucrose 50.

**Sys Specific.** An Indian cure for sprue, dysentery and diarrhoea. It consists of "powders" containing principally calcium carbonate—one to be mixed with 12 ounces of water and laudanum to be added, if necessary.

**Trochisci Antacidi (B.P.C.)** contain calcium carbonate  $3\frac{1}{2}$  gr., heavy magnesium carbonate  $2\frac{1}{2}$  gr. and sodium chloride 1 gr.

**Unguentum Cretæ (B.P.C.).** 20% in spermaceti ointment.

**Os Sepiæ (B.P.C.).** Cuttle Fish Bone. The internal shell of *Sepia officinalis* (Cephalopoda). Contains 80 to 85% of calcium carbonate, and is used as a mild abrasive in tooth powders.

**Sepia** is prepared from the fluid in the ink gland of the cuttle fish by drying dissolving in alkali and reprecipitating with acid. Is used in homœopathy.

**Calcii Gluconas** (*B.P. Add. I, U.S.P. XI, Fr. Cx., P. Ned. V. Supp. II*).  $[\text{CH}_2\text{OH} \cdot (\text{CHOH})_4 \cdot \text{COO}]_2\text{Ca} \cdot \text{H}_2\text{O} = 448.4$ .

*Dose*.—30 to 60 grains (2 to 4 g.). *U.S.P. XI* average doses—oral, 75 gr.; intravenous, 15 gr.

A white crystalline and granular powder, *soluble* 1 in 30 of water, 1 in 5 of boiling water; insoluble in alcohol and ether. Contains 8.9% of calcium. Gluconic acid,  $\text{C}_6\text{H}_8(\text{OH})_5\text{COOH}$ , is formed by oxidation of glucose, sucrose, dextrin or starch. Quantitative yields are obtained by the action of *Bact. suboxydans* on glucose. It is a syrupy compound soluble in water.

It is administered parenterally in an approximately 10% solution prepared by dissolving 10 g. of calcium gluconate in 95 ml. of water, filtering whilst hot and autoclaving. The solution should be stored in sealed ampoules and must be free from all solid particles, otherwise it will crystallise. Proprietary concentrated solutions of calcium gluconate are supersaturated solutions stabilised by patented methods.

The presence of calcium glucoheptonate increases the solubility of calcium gluconate, and the following solution has been proposed for use as an injection:—Calcium gluconate 73.35 g., calcium glucoheptonate 30 g., water to 1000 g. Boil, filter, fill into ampoules and sterilise for 1 hour at 100°.

A 10% solution which will not crystallise may be prepared by adding 2020 g. of boiling distilled water to 200 g. of calcium gluconate, filtering through a hard filter paper in a covered funnel, heating the filtrate in an autoclave for 30 minutes at 112°, filtering through a No. 4 sintered glass filter and transferring to washed and dried ampoules which are then sealed and heated to 112° for 30 minutes on three successive days.—L. Bracaloni, *per Quart. J. Pharm.*, 1937, 117.

Solutions containing an amount of calcium methionate equal to or greater than calcium gluconate yielded relatively stable solutions containing from 7 to 70% of gluconate.—G. L. Jenkins, *J. Amer. pharm. Ass.*, 1938, 484.

10% solutions can be prepared by the addition of camphorsulphonic acid 1%.—G. Lusignani, *Boll. Chim. farm.*, 1940, 79, 137.

**Uses.** Taken by the mouth, it is well absorbed. Intravenously it is better tolerated than calcium chloride. The acid-base factor is eliminated. Intramuscularly it is painless and non-irritant. It influences many respiratory diseases, relaxing bronchial spasm and decreasing secretion of mucosa of the respiratory tract. Intramuscularly it is of value in serum sickness, urticaria; spasmodic croup and infantile convulsions. Also used in debility, malnutrition and neurasthenia. Injections of calcium gluconate should not be given during the course of treatment with the digitalis group.

**ECLAMPSIA.** Hyperguanidinæmia is associated with hypocalcæmia. 7 g. (total) of calcium gluconate intravenously, intramuscularly and subcutaneously, cured in 24 hours. Eclamptic syndrome yields to calcium medication.—*Brit. med. J. Epit.*, ii/1930, 42.

**MILK FEVER** cured by injecting calcium gluconate: also prophylactic.—*Lancet*, ii/1930, 411.

**EDEMA** of children suffering from nephrosis treated.—*Brit. med. J. Epit.*, i/1931, 102.

**SERUM SICKNESS.** The following treatment was given in 15 cases as soon as a rash developed. 10 or 20 ml. of 20% calcium gluconate intravenously, supplemented by 10 ml. of 10% calcium gluconate intramuscularly, and the intramuscular injection repeated 12-hourly till rash or symptoms subsided;

the solution for intravenous injection was warmed to body temperature and injected slowly (10 ml. in 2 or 3 minutes). As compared with 15 control cases (treated with adrenaline subcutaneously, ephedrine *per os*, calamine lotion locally, and sedatives), the rash in those treated with calcium lasted only 2.9 days against an average of 5.4 days, and subjective symptoms (itching, arthralgia, headache, cramps, nausea, etc.) 3.3 against 7.1 days.—T. J. Curphey and S. Solomon, *New Engl. J. Med.*, 1936, 214, 148.

**Calcium L-B** (*Allen & Hanburys, London*). Calcium lactobionate. Supplied in solution in ampoules, 2 g. in 5 ml. For intramuscular or subcutaneous injection in calcium deficiency. Also combined with parathyroid in tablets and elixir.

**Calcium Sandoz** (*Sandoz Products, London*). Preparations of calcium for oral, intramuscular or intravenous administration. Oral preparations contain calcium gluconate and are available as powder, chocolate-flavoured tablets (25 gr.), effervescent tablets (60 gr.) or syrup (60 gr. in  $\frac{1}{2}$  oz.). Preparations for injection contain calcium glucono-gallacto-gluconate, which is soluble in water to form a perfectly stable solution. It is available in 2, 5 or 10 ml. ampoules of a 10% solution for intramuscular use, or in 5 or 10 ml. ampoules of a 20% solution for intravenous use.

**Glucocalcium** (*Lilly, London*). Combination of calcium with glucose degradation products. *Dose*.—3 to 5 ml. intramuscularly and 5 to 20 ml. intravenously. Tuberculosis, asthma, hay fever, etc.

**Percalcin** (*Evans, Sons, Lescher & Webb, Liverpool*). A stable solution of calcium in organic combination containing the equivalent of 4% w/v of calcium hydroxide ( $2\frac{1}{2}$  times the strength of 10% calcium gluconate). It may be administered either intravenously or intramuscularly in the treatment of calcium deficiency. Intravenously the dose is 4 to 25 ml. of warm solution given slowly; intramuscularly, 2 to 4 ml. daily. For pulmonary tuberculosis the dose is 5 ml. intravenously 2 to 3 times per week, increased gradually to 20 ml.

**Selvorol** (*Bayer Products, London*). Calcium salt of glucohexatric acid containing 8.5% of Ca. Administered orally in doses of 30 gr. twice daily. Asthma, hay fever, urticaria and calcium deficiencies.

**Calcii Lævulus**. *Syn.* CALCIUM LÆVULINATE.  
( $\text{CH}_3 \cdot \text{CO} \cdot \text{CH}_2 \cdot \text{CH}_2 \cdot \text{COO}$ )<sub>2</sub>Ca,  $2\text{H}_2\text{O} = 306.2$ .

*Dose*.—15 grains (1 g.) by intravenous injection in a 10% solution. 5 grains (0.3 g.) by intramuscular injection in a 15% solution.

A white, crystalline, almost odourless powder with a slightly bitter taste. Its calcium content is 50% higher than that of calcium gluconate.

*Soluble* 1 in 2.5 of water.

**Levu-Calcin** (*Glaxo Laboratories, London*). Calcium levulinate solution for injection either intravenously (10%) in 10 ml. ampoules or intramuscularly (15%) in 2 ml. ampoules.

**Tetanol** (*Crookes' Laboratories, London*). A solution of calcium levulinate. *Dose*.—Intravenously, 5, 10, or 20 ml. 13% solution; intramuscularly, 2 ml. 20% solution.

**Calcii Hydroxidum** (*B.P., U.S.P. XI, Fr. Cx.*). *Syn.* CALCIUM HYDRAS.  $\text{Ca}(\text{OH})_2 = 74.10$ . Should be recently made by action of water on calcium oxide. Is more soluble in cold water than in hot.

**Linimentum Calcii Hydroxidi** (*B.P.C.*).

Solution of calcium hydroxide 1, olive oil 1.

**Linimentum Calcii Hydroxidi cum Oleo Lini** (*B.P.C.*).

*Syn.* CARRON OIL.

Solution of calcium hydroxide 1, linseed oil 1. Eucalyptus oil 1 to 2% is sometimes added as antiseptic.

Carron oil was at one time extensively used for the treatment of burns, but with the introduction of tannic acid therapy it fell into disuse. With the recent re-introduction of oily preparations for burn dressings there is a possibility of its return to favour. In a series of controlled animal experiments Thomson (*Lancet*, i/1941, 341) has shown that healing is promoted and regeneration of damaged tissue occurs with greater ease when burns are treated with carron oil than when treated with tannic acid.

**Liquor Calcii Hydroxidi (B.P.).** *Syn.* LIQUOR CALCIS, AQUA CALCIS (*Fr. Cx.*), LIME WATER.

*Dose.*—1 to 4 ounces (30 to 120 ml.).

Contains not less than 0.15% *w/v* of  $\text{Ca(OH)}_2$ . It is given with milk to infants to prevent formation of large clots.

**Liquor Calcii Hydroxidi Saccharatus (B.P.C.).** *Syn.* LIQUOR CALCIS SACCHARATUS.

*Dose.*— $\frac{1}{4}$  to 1 drachm (1 to 4 ml.).

Contains the equivalent of 2.4% *w/v* of  $\text{Ca(OH)}_2$  with sucrose and water.

**Liquor Calcii Hydroxidi (U.S.P. XI).**

*Average dose.*— $\frac{1}{2}$  ounce (15 ml.).

Same as B.P., but made with 3 g. of calcium hydroxide for each litre of solution.

**Calcii Oxidum (Fr. Cx.).** *Syn.* QUICKLIME, CALCARIA USTA (*P. Jap. V*).

White or greyish-white masses. Used as a caustic, *e.g.*, in *Pasta Londinensis (q.v.)*. Soda-lime is prepared by slaking quicklime with sodium hydroxide solution and heating to redness.

**LIME BURNS.** A 4% solution of ammonium chloride is more effective than any solutions hitherto generally employed, and has been tried out in a series of cases with considerable success. It is no more painful to the eye than other irrigating fluids. The preliminary application of an analgesic solution and the removal of large particles by means of a camel-hair brush dipped in a mixture of Vaseline and paraffin, should also form part of the first-aid treatment.—G. C. Pether, *Brit. med. J.*, i/1939, 668.

**Calcii Saccharas.** *Syn.* CALCIUM MONOSACCHARATE.

$\text{C}_{12}\text{H}_{22}\text{O}_{11}\text{CaO} = 398.2$ .

*Dose.*—8 to 30 grains (0.5 to 2 g.).

In colourless tufts, soluble in water. An antacid for dyspepsia, specially for children; also as an antidote to carbolic acid poisoning in 10 times above doses.

**Calcii Sulphas Exsiccatus (B.P.C., P. Helv. V, P. Jap. V).** *Syn.* PLASTER OF PARIS, CALCIUM SULPHATE (*Fr. Cx.*).

$\text{CaSO}_4 \cdot \frac{1}{2}\text{H}_2\text{O} = 145.1$ . A white, hygroscopic, odourless powder. Two pounds require about 1 pint of water; this sets rapidly and firmly.

Moistening with 5% dextrin solution makes a strong dressing but sets slowly. Sodium chloride 1% added hastens setting but 2% retards.

**Ligamentum Calcii Sulphatis (B.P.C.).** Plaster of Paris bandages consist of bleached cotton cloth impregnated with the plaster and suitable adhesives.

**Calx Sulphurata (B.P.C.).** *Syn.* CALCII SULPHIDUM CRUDUM, CANTON'S PHOSPHORUS. Contains not less than 50% of  $\text{CaS} = 72.14$ .

*Dose.*— $\frac{1}{4}$  to 1 grain (0.016 to 0.06 g.) in pill.

Is prepared by reducing calcium sulphate with charcoal. A greyish powder with odour of hydrogen sulphide. Sparingly *soluble* in water with decomposition.

**Uses.** Largely used for boils, carbuncles, acne and scrofulous sores. Continued administration is stated to act as a prophylactic against puerperal sepsis. It rarely purges even in 2 grain doses thrice daily. Some give small doses *every hour*. In strumous ophthalmia, as well as in periostitis and alveolar abscesses, has been found of service. Also in follicular tonsillitis. For boils give 1 grain *t.d.*, increased to 8 grains *p.d.*

**ACNE.** Good results claimed with doses of not less than 2 grains 3 times a day.—A. Whitfield, *Brit. J. Derm.*, 1934, 257.

**PUERPERAL SEPSIS.** Calcium sulphide in doses varying from  $1\frac{1}{2}$  to 12 grains per 24 hours reduced the death-rate from sepsis in the County Maternity Hospital, Bellshill, Lanark, from 5.3 per 1000 in cases confined within the institution from 1927 to 1933 inclusive (5421 cases) to 0.7 per 1000 for 1933 to 1935 inclusive (2518 cases). Used either as a prophylactic previous to confinement or even during the puerperium, it not only prevents the incidence of puerperal infection, but also does much to curtail the mortality.—H. J. Thomson, *Brit. med. J.*, ii/1935, 1070.

Calcium sulphide usually given as a pill in doses of 3 gr. twice daily, increased to four times a day in complications such as toxæmia of pregnancy, hæmorrhage, etc. Only 14 cases of puerperal sepsis and 11 of puerperal pyrexia with 1 death in more than 2000 unselected confinements, of which about 40% were admitted as emergencies.—H. J. Thomson, *Brit. med. J.*, ii/1936, 70.

**Liquor Calcis Sulphuratæ (B.P.C.).** *Syn.* LOTIO CALCIS SULPHURATÆ, VLEMINCKX'S SOLUTION, CALCIUM SULFURATUM SOLUTUM (*P. Helv. V*).

Prepared by boiling sulphur with calcium hydroxide and water, and contains polysulphides of calcium equivalent to 4 to 5% *w/v* of sulphur.

Valuable in Dhobie's itch; at first used diluted 3 or 4 times.

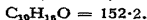
For eczematous itching, baths of the solution, 1 tablespoonful to every 7 gallons of water, have been used.

**Colloidal Calcium.** Preparations of colloidal calcium usually contain the metal in the form of a compound. The usual strength is 1 in 2000.

**Dose.**—8 to 15 minims (0.5 to 1 ml.) hypodermically;  $\frac{1}{2}$  to 1 drachm (2 to 4 ml.) orally. Is used for the general purposes of calcium therapy.

## CAMPHORA

*B.P., U.S.P. XI, Fr. Cx., P. Helv. V, etc.*



**Dose.**—2 to 5 grains (0.12 to 0.3 g.); 1 to 3 grains (0.06 to 0.2 g.) by subcutaneous injection.

Camphor is a white crystalline substance obtained from *Cinnamomum Camphora* (*Lauraceæ*) in Formosa and Japan (natural camphor), or obtained synthetically from the pinene of oil of turpentine (synthetic camphor). *M.p.* 174° to 177°; *b.p.* 204°.



Natural camphor is dextrorotatory, whilst synthetic camphor is optically inactive. Both forms are official.

Camphor is sold in balls, and in  $\frac{1}{2}$ ,  $\frac{1}{4}$ ,  $\frac{1}{8}$ , 1 and 4 ounce cubes, also as **Flowers of Camphor**. The latter is a convenient form for dissolving.

**Soluble** 1 in 700 of water, 1 in  $1\frac{1}{2}$  of alcohol 90% (more soluble in dehydrated alcohol), 12 in 7 of ether, about 4 in 1 of chloroform, 2 in 1 of glacial acetic acid, 1 in 3 of olive oil, and 1 in 1.5 of oil of turpentine. Also soluble in other fixed and volatile oils, but insoluble in glycerin.

Camphor, when mixed in certain proportions with many crystalline substances, causes mutual liquefaction of the two—e.g., camphor 4, phenol 12, and water 1; camphor 1 and chloral hydrate 1; camphor 2 and menthol 3; camphor 1 and thymol 1; camphor 2 and  $\beta$ -naphthol 1; camphor 2 and salol 3; camphor and butyl-chloral hydrate liquefy when heated, but solidify on cooling; so will camphor 84 and salicylic acid 65. Camphor is powdered by rubbing with a few drops of alcohol.

**Antidotes.** Empty stomach by emetic or stomach tube. Give purgative dose of magnesium sulphate in plenty of water. Keep patient warm, and give inhalations of ether or dilute ammonia. Stimulants, e.g., digitalin  $\frac{1}{2}$  gr., strychnine  $\frac{1}{8}$  gr., caffeine sodium benzoate 2 gr., hypodermically.

**Caution.** It is dangerous to place camphor or menthol, e.g., a 20% ointment, into the nostrils of an infant. A small quantity applied in this way may cause immediate collapse with signs of a severe syncopal attack.

**Poisoning** from 75 grains of camphor as camphorated oil. Recovery: Stomach washed out and several ounces concentrated magnesium sulphate solution left in.—J. Cottrell, *Brit. med. J.*, i/1931, 96.

**Uses.** Internally it is sedative, anti-spasmodic, carminative, expectorant, diaphoretic, anaphrodisiac and antipyretic. It is given internally to abort colds in the head, to relieve hiccough, for whooping cough, chordee and lumbago. For arteriosclerosis and for old patients with heart trouble continued use of camphor internally is of value. Is injected as a stimulant for patients *in extremis*, though its action on the circulation is inconstant and unreliable.

It is no exaggeration to say that experienced pharmacologists would find great difficulty in supporting the claims of clinicians that camphor in oil is a powerful stimulant of respiration and circulation. It is difficult to assess the value of its use in collapsed and moribund patients.—E. C. Dodds, *Proc. R. Soc. Med.*, 1936, 29, 656.

Natural camphor and certain synthetic products are definitely depressant upon the heart and circulation in experimental animals. If, however, weak concentrations of camphor are kept in contact with the heart or other living tissue for a certain length of time and then used for injection, a slight but definite stimulant effect is obtained. It is suggested that when camphor comes in contact with a living tissue certain slow biochemical changes take place, so that the clinical effect of cardiac stimulation is observed. It is probable that the chemical change occurs in the liver.—R. N. Chopra, J. S. Chowhan and N. De, *Indian J. med. Res.*, 1936, July, 249.

**ENGORGEMENT OF BREASTS.** Intramuscular injections of  $1\frac{1}{2}$  grains of value. Has inhibiting action on milk secretion. Give two injections the first day and

one for each of next three days.—W. Philphot, *J. Amer. med. Ass.*, ii/1929, 65.

Camphor in oil does not inhibit lactation or hasten the process of involution in the rat or the guinea-pig. Until more adequately controlled and more objectively measured experiments on the human being are presented, the advisability of the use of such a substance is open to question.—R. R. Greene and A. C. Ivy, *J. Amer. med. Ass.*, i/1938, 641.

**Camphor Ball.** Spermaceti 4, white wax 12, almond oil 5; melt in a water-bath and add flowers of camphor 4. Dissolve, and when nearly cold pour into moulds. Useful for chapped skin.

**Aqua Camphoræ (B.P.).** *Syn.* CAMPHOR JULEP, MIST. CAMPHORÆ. 1 in 1000. 60 minims of spirit of camphor added to 12 oz. of water gives a solution of approximately the same strength. Camphor water (*U.S.P. XI*) is a saturated solution.

**Aqua Sedativa.** *Syn.* EAU SÉDATIVE, LOTION AMMONIACALE CAMPHRÉE (*Fr. Cx.*). Spirit of camphor (10%) 10, sodium chloride 60, solution of ammonia 60, distilled water 1000, all by weight.

As a compress for migraine and rheumatism, and to contusions.

**Aqua Camphoræ Concentrata (B.P.C.).**

*Dose.*—5 to 15 minims (0.3 to 1 ml.). 1 part equals 40 parts of camphor water.

**Elixir Camphoræ.** *Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Spirit of camphor 10, syrup 5, distilled water 1. Contains 1 in 16. It mixes and diffuses well in water.

**Injectio Camphoræ (B.P.C.).** *Syn.* HUILE CAMPHRÉE STÉRILISÉE INJECTABLE (*Fr. Cx.*).

*Dose.*—8 to 30 minims (0.5 to 2 ml.).

10% w/v in olive oil.

In pneumonia 25 minims has been given as a general rule to start with, but much larger doses have been employed—even 12 ml. of a 20% solution.

**Injectio Camphoræ Ætherea (B.P.C.).** *Syn.* CURSCHMANN'S SOLUTION.

*Dose.*—4 to 15 minims (0.25 to 1 ml.).

Camphor 20% w/v and ether 30 v/v in olive oil.

*Caution.* Various amounts (30 to 300 ml.) of 1 to 10% solution have been injected. A case recorded of acute poisoning from 170 ml. of 10% solution after an operation. 1% may be safe and not more than 300 ml. of this solution. Urticaria has followed the use of injections.

**Injectable Camphoræ Æthereus (P. Helv. V).** *Syn.* ÆTHER CAMPHORATUS. Camphor 1 g., anæsthetic ether to 10 ml.

[P1] **Linctus Camphoræ Compositus (B.P.C.).**

*Dose.*— $\frac{1}{2}$  to 2 drachms (2 to 8 ml.).

Camphorated tincture of opium, 1 in 4, in a wild cherry, squill and senega menstruum.

**Linimentum Camphoræ (B.P.).** *Syn.* CAMPHORATED OIL, OLEUM CAMPHORATUM (*P. Dan., P. Jap. V*).

Camphor 20% w/v in olive oil. Olive oil is not the most satisfactory oil for this liniment. It congeals and is often rancid, and could, with advantage to suppliers and users, be replaced with arachis oil.

*B.P. Add. II* allows the use of either arachis, cottonseed, or sesame oil, in place of olive oil, in making liniment of camphor.

*Huile Camphrée* (*Fr. Cx.*) is 10% in olive or arachis oil.

*Linimentum Camphoræ* (*U.S.P. XI*). 20% *w/w* of camphor in cottonseed oil.

Cottonseed oil unsatisfactory for camphor liniment. Likely to congeal to consistence of cheese.—*J. J. Blackie, Pharm. J.*, i/1931, 17.

[P2] *Linimentum Camphoræ Ammoniatum* (*B.P.*). *Syn.* LINIMENTUM CAMPHORÆ COMPOSITUM.

Camphor 12.5% *w/v*, strong solution of ammonia 25% *v/v* and oil of lavender in alcohol or methylated spirit.

*Linimentum Camphoræ et Saponis* (*U.S.P. XI*).

Camphor 4.5% and hard soap 6%, with oil of rosemary, in alcohol and water.

[P1] *Pigmentum Camphoræ Chloral et Menthol*.

Camphor, chloral hydrate and menthol, equal parts. Useful in acute fibrositis, rubbed in gently with the fingers.

*Pilula Camphoræ*.

To form camphor into pills use  $\frac{1}{2}$  its weight of powdered curd soap and a few drops of alcohol, or a little lard in a warm mortar.

*Spiritus Camphoræ* (*B.P.*).

*Dose*.—5 to 30 minims (0.3 to 2 ml.).

Contains 10% *w/v* of camphor in alcohol 90%.

*Spiritus Camphoræ* (*U.S.P. XI*).

*Average dose*.—15 minims (1 ml.).

Camphor 9.2 to 10.4% *w/v* in alcohol.

*Æther Spirituosus Camphoratus* (*P. Dan.*). *Syn.* KAMFERDRAABER. 10% *w/w* in spirit of ether 25% *w/w*.

*Spiritus Camphoræ Fortior*. *Syn.* RUBIN'S SOLUTION.

Flowers of camphor 1, absolute alcohol (by weight) 1. *Dose* for diarrhoea.—2 to 5 drops on sugar every 5, 10 or 15 minutes, according to the severity of the symptoms.

[P1] *Syrupus Camphoræ Compositus* (*B.P.C.*).

*Dose*.— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Contains  $\frac{1}{10}$  gr. of camphor and 1 m. of tincture of opium with oil of anise, benzoic acid, glacial acetic acid, vinegar of ipecacuanha and vinegar of squill in a syrup basis to 1 dr.

*Tablets of Camphor and Quinine*. Camphor  $\frac{1}{2}$  gr., with quinine acid sulphate 1 gr. To check catarrh and as a tonic.

*Teinture de Camphre Concentrée* (*Fr. Cx.*). Camphor 10% *w/w* in alcohol 90%.

*Teinture de Camphre Faible* (*Fr. Cx.*). Camphor 2.5% *w/w* in alcohol 60%.

*Unguentum Camphoræ* (*B.P.C.*). 10% in white soft paraffin. *Fr. Cx.* has 20% in a base of benzoinated lard and white beeswax.

*Unguentum Camphoræ Durum* (*B.P.C.*). *Syn.* CAMPHOR ICE. 6% in hard and soft paraffins.

*Acidum Camphoricum* (*B.P.C.*, *P. Ned. V*, *P. Helv. V*, *P. Jap. V*, *F.E. VIII*).  $C_8H_{14}(COOH)_2 = 200.2$ .

*Dose*.—8 to 30 grains (0.5 to 2 g.) in cachets or suspended with tragacanth in a mixture.

Formed on oxidation of camphor with nitric acid. Odourless crystals, dextrorotatory, m.p. 185° to 187°.

**Soluble** about 1 in 160 of water, about 1 in  $1\frac{1}{2}$  of alcohol 90% and 1 in 10 of fatty oils; also soluble in ether, but only slightly in chloroform.

**Uses.** Has been advocated for use in night sweats of phthisis, but its action is doubtful; also in cystitis by intravesical injections of 2% aqueous solution with 11% alcohol, and as an intestinal disinfectant. Further in solution as a local astringent for nose and throat. In skin affections saturated solution in dilute alcohol locally useful.

**Camphoræ Monobromidum** (*B.P.C.*, *P. Helv. V*, *P. Ital. V*, *P. Jap.*, *F.E. VIII*, *P. Belg. IV*, and *P. Ned. V*). *Syn.* CAMPHORA MONOBROMATA, 3-BROMOCAMPHOR.  $C_{10}H_{15}OBr = 231.0$ .

**Dose.**—2 to 8 grains (0.12 to 0.5 g.), in pills with  $\frac{1}{2}$  of its weight of curd soap and proof spirit *q.s.*, or dissolved in oil and emulsified.

In colourless prisms with persistent camphoraceous taste. **Soluble** 1 in 12 of alcohol 90%, 1 in 2 of ether, 10 in 7 of chloroform, 1 in 8 of olive oil, sparingly soluble in glycerin, soluble in sulphuric acid with formation of nearly colourless solution. It is used as a hypnotic, and is of value in epileptic vertigo, cases of petit mal, chorea, hysteria, delirium tremens, whooping cough and asthma, and for erections in gonorrhœa.

**Elixir Camphoræ Monobromatæ.**

Camphor monobromide 1, spirit of cinnamon (1 in 10) 10; dissolve and add red elixir 60, syrup *q.s.* to 100. **Dose.**— $\frac{1}{4}$  ounce.

Enuresis is treated with this combined with belladonna, where potassium bromide is unsuitable.

**Camphemyl** (*Ciba, London*). 10% solution of camphor in a mixture of methyl urethane, monoethyl urea and distilled water. An improvement on oily solutions.

**Camphro-Salyl** (*Fraisse, Paris; Wilcox, Jozeau, London*). Ampoules contain benzyl salicylate 0.5 g., camphor 0.1 g., in olive oil 5 ml. **Dose.**—5 ml. injected into the sciatic nerve. For the relief of pain in sciatica, neuritis and lumbago.

**Sodii Camphorsulphonas.** *Syn.* SODIUM CAMPHOSULPHONATE.  $C_{10}H_{15}OSO_3Na = 254.28$ .

**Dose.**—2 to 5 grains (0.15 to 0.3 g.) by subcutaneous, intramuscular or intravenous injection in the form of a 15% aqueous solution.

A white crystalline substance, readily **soluble** in water.

**Uses.** This possesses the stimulating action of camphor on the respiration and circulation, but has the advantage over camphor in oil solution that it is more rapidly absorbed and has only very slight toxicity. It is employed in the treatment of heart failure, syncope and shock, in cases of poisoning by carbon monoxide, gas, narcotics, etc., and in collapse during narcosis.

Salts of camphosulphonic acid have given satisfactory clinical results in cardiopathy. Directions are given for preparing camphosulphonic acid, its quinine, calcium and magnesium salts and concentrated solutions of the latter for hypodermic injection.—*per Pharm. J.*, i/1938, 53.

The slight, but definite, action of camphor on respiration and the cardiovascular system is rendered surer through even distribution and absorption. Its use

has been recommended in cases in which stimulation of a patient who is to receive a transfusion is required.—E. C. Dodds, *Proc. R. Soc. Med.*, 1936, 29, 656.

**Cardatone** (*Evans, Sons, Lescher & Webb, Liverpool*). An aqueous solution containing 15% of sodium camphor-sulphonate. A non-toxic analeptic for use as a cardiac and respiratory stimulant.

*Dose*.—1 or 2 ml. subcutaneously, intramuscularly or intravenously, or 1·5 to 6 ml. of a special solution *per os*. In cases of poisoning by carbon monoxide, gas, narcotics, etc., as much as 5 to 15 ml. may be given intravenously; in collapse during narcosis, 2 to 6 ml. may be injected intravenously followed by up to 5 ml. intramuscularly.

**Calcium Camphorsulphonate**. ( $C_{16}H_{15}OSO_3$ )<sub>2</sub>Ca = 502·6. A white, amorphous or minutely crystalline powder, very soluble in water and alcohol, but sparingly soluble in ether. Its solutions are very stable and may be sterilised by heating at 112° for 30 minutes.

The use of this salt, by reason of its stimulant action in depressive states, and because it diminishes bronchial secretion and lessens sweating in pre-tubercular states and tuberculosis, will increase.—R. Bozzola, *per Pharm. J.*, 1/1938, 53.

**Chinocal** (*Richter, London*). Ampoules contain calcium camphorsulphonate 8 gr., quinine hydrochloride  $\frac{1}{2}$  gr., in distilled water 5 ml. *Dose*.—5 ml. once or twice daily rectally or intravenously. In diseases of the upper respiratory tract and for the induction of labour.

**Magnesium Camphorsulphonate**. ( $C_{16}H_{15}OSO_3$ )<sub>2</sub>Mg = 486·9. A white crystalline substance, soluble in water, sparingly soluble in alcohol, but insoluble in ether.

Magnesium camphorsulphonate may advantageously be employed in association with the calcium salt, because of its stabilising action. A solution containing 20% of calcium camphorsulphonate and 10% of magnesium camphorsulphonate sterilised at 112° for 30 minutes, was unaltered and neutral in reaction.—R. Bozzola, *per Pharm. J.*, 1/1938, 53.

**Solucamphre** (*Delalande, Paris; Roberts & Co., London*). Water-soluble camphor. 14% solution of *d*-camphor sulphonate of diethylenediamine. *Dose*.—1 to 3 injections of 5 ml. daily subcutaneously or intramuscularly, or an injection of 2 to 5 ml. intravenously in urgent cases. Also as drops, 50 to 100 daily. To replace camphor in oil as a cardiac and respiratory stimulant.

**Leptazolium** (*B.P. Add. III*). *Syn.* METRAZOL.  
( $CH_2$ )<sub>5</sub>C·N<sub>4</sub> = 138·1.

*Dose*.— $\frac{2}{3}$  to 1½ grains (0·05 to 0·1 g.).

Leptazol is pentamethylenetetrazol, a white, crystalline powder with a bitter taste; m.p. 57° to 60°.

Freely *soluble* in water, alcohol, chloroform and ether, giving neutral solutions. Aqueous solutions may be sterilised by autoclaving.

**Uses**. Leptazol has a powerful action on the vasomotor and respiratory centres, and is thus a powerful cardiac and respiratory stimulant. It is usually employed by injection (*vide infra*) either subcutaneously, intramuscularly or intravenously, but in less urgent cases it gives good results by the mouth, the average dose being 1½ gr. three or four times daily. (Alternatively, a dose of 1 ml. of the 10% solution may be given orally.)

**Injectio Leptazoli** (*B.P. Add. III*).

*Dose*.—8 to 15 minims (0·5 to 1 ml.), by subcutaneous injection; 30 to 75 minims, increasing to 180 minims (2 to 5 ml., increasing to 12 ml.), by intravenous injection as a convulsant.

Leptazol 10 g., sodium phosphate 0·25 g., in distilled water to 100 ml., with sufficient dilute hydrochloric acid or sodium hydroxide to give a pH of 7·8. The addition of an antiseptic to the

solution when dispensed in multiple-dose containers is not allowed.

**Uses.** Its action is produced smoothly and is of great value in a dose of 1 ml. subcutaneously, in cardiovascular collapse, shock and respiratory depression.

It is also of value in the treatment of barbiturate poisoning and anæsthetic narcosis, for which purpose it is given by slow intravenous injection in a dose of from 3 to 5 ml.

In addition to the foregoing, it has been widely employed for the convulsant treatment of schizophrenia, starting with a dose of 5 ml. intravenously and increasing by 1 ml. until a fit occurs. It should be pointed out, however, that the treatment, though producing valuable results, is both unpleasant and dangerous (the violence of the convulsions may cause fractures of the limbs or vertebræ), and should be carried out only in a fully equipped mental hospital.

**ANÆSTHETIC NARCOSIS.** Observations on 96 patients who had been anæsthetised with Evipan, ether, or Avertin, and who had been awakened by an intravenous injection of 5 ml. of Cardiazol. In most cases the effect was very prompt; even during the injection, which was given very slowly, the respiration became deeper and in some cases more frequent, the pulse meanwhile becoming stronger and more regular. The improvement thus effected in the action of the heart was so marked in some cases that, although a saline infusion had previously seemed necessary, it now became superfluous. With the exception of four cases (abdominal operations) there was an appreciable shortening of the post-operative unconsciousness, and thus the risk of aspiration accidents was reduced.—Pieniezny, *Dtsch. med. Wschr.*, 1935, 1641.

**SCHIZOPHRENIA.** Convulsive treatment with Metrazol (Cardiazol) is of value in the treatment of patients with dementia præcox, particularly when the duration is not of more than two years. The rate of remission is almost inversely proportional to the duration of the psychosis. 85% of patients whose symptoms were less than six months in duration had a remission. The type showing the greatest tendency to remit is the catatonic, followed closely by the paranoid. The treatment is given in the morning on an empty stomach. The dose is the smallest amount of the drug that will produce a typical convulsive seizure. The first dose ranges from 2 to 5 ml. of a 10% solution, which usually produces a convulsion. When the convulsive dose is reached it is maintained until it fails to give a reaction. The injections are given two or three times a week until the patient shows a remission, the treatment being resumed if there is a relapse. Contraindications are acute infectious diseases, pulmonary disease and cardiovascular disorders.—I. Finkelman *et al.*, *J. Amer. med. Ass.*, i/1938, 706.

Vertical and lower limb fractures may be completely eliminated by giving a spinal anæsthetic (10 mg. of Pontocain hydrochloride or 100 mg. of Novocain, dissolved in 4 ml. of cerebrospinal fluid obtained by lumbar puncture). Large doses of Cardiazol may be avoided by a preliminary intravenous injection of 0.5 ml. of adrenaline solution; at the moment of facial blanching half the usual dose of Cardiazol is injected and the result equals that of the full dose.—A. E. Bennett, *Amer. J. med. Sci.*, 1939, 198, 695.

Cardiazol is a valuable means of treatment. Of 34 patients treated 12 recovered, 10 improved and 12 showed no improvement. Compared with other methods of shock treatment, Cardiazol therapy is relatively safe. It seems to exert its maximum beneficial effect on early cases of mental disorder characterised by emotional and intellectual blocking and reduced psychomotor activity, but without severe destruction of nerve cells.—M. V. Govindaswamy, *Lancet*, i/1939, 506.

Statistical data of 2011 cases. Recovery rate sufficiently high to justify Cardiazol treatment.—F. Reitmann, *Lancet*, i/1939, 439.

From a consideration of 218 cases of schizophrenia it was concluded that there is no significant difference in the numerical results obtained by ordinary hospital treatment, hypoglycæmic treatment and convulsant treatment. Hypoglycæmia

gives the best results in the paranoid sub-group. Convulsion therapy appears to be best suited for stupor reactions. The special treatments offer the best chance of recovery to a potentially recoverable patient whose illness is dragging on. They reduce the average duration of hospital treatment.—H. Stalker, *Lancet*, i/1939, 437.

In patients undergoing convulsion therapy with Cardiazol or Triazol, the development of resistiveness, fear and panic during treatment has been noted. Sedatives such as morphia, hyoscine and the barbiturates, proved unsatisfactory in allaying these symptoms. Insulin premedication not only proved effective in obtaining co-operation in 22 resistive patients, but also reduced the incidence of confusion and excitement of recovery from the induced fits. A scheme of stepping up the dosage is employed similar to that used in insulin shock. The patient is started with 10 units and the injection increased by tens until the desired co-operation is obtained.—D. E. Sands, *Lancet*, ii/1939, 250.

Aqueous or alcoholic extract of curare in physiologic dosage intravenously sufficient to produce flaccid generalised motor paresis adequately protects the patient from traumatic complications of convulsive shock therapy.—A. E. Bennett, *J. Amer. med. Ass.*, i/1940, 322.

**STUPOR.** It would appear advisable to treat every case of stupor, whether of long or short duration, with Cardiazol. Complete recovery or improvement may be expected in those cases in which the illness has lasted a relatively short time and in which the stupor has been almost the earliest symptom. A 10% solution of Cardiazol, buffered to pH 8 with 0.1% disodium hydrogen phosphate, is injected intravenously, beginning with 0.5 g. in the case of men, and 0.4 g. in the case of women. Three injections are given weekly and the dose increased by 0.1 g. whenever a larger amount is required to produce a convulsion.—J. S. Harris and C. R. Birnie, *Brit. med. J.*, ii/1938, 449.

**Cardiazol (Knoll, London).** Preparations of leptazol issued as liquid (1 ml. ampoules and 10 ml. bottles), tablets (1½ gr.) and powder; for the treatment of narcosis it is available in 3 ml. ampoules, and for convulsion therapy in 5 ml. ampoules or 50 ml. bottles.

[P1-81] **Cardiazol-Dicodid Drops (Knoll, London).** 20 drops correspond to about 1½ gr. of Cardiazol and ½ gr. of dicodid hydrochloride (*exempt* [D]). *Dose.*—Start with small doses to establish tolerance; infants and young children 2 to 5 drops 2 to 3 times daily, older children 5 to 10 drops 3 times daily, adults 10 to 20 drops. Cough, whooping cough, asthmatic and stenocardiac conditions.

[P1] **Cardiazol-Ephedrine**, a combination of Cardiazol with ephedrine hydrochloride, for bronchial asthma, circulatory collapse and collapse during narcosis. Each tablet or each ml. of solution contains ½ gr. of ephedrine hydrochloride and 1½ gr. of Cardiazol.

**Cardiazol-Quinine.** Tablets contain ½ gr. of Cardiazol and 1½ gr. quinine hydrochloride (*dose.*—2 to 3 daily); ampoules of 1 ml. contain 1½ gr. of Cardiazol and 4 gr. of quinine lactate in aqueous solution (*dose.*—2 to 3 daily intramuscularly); suppositories contain 1½ gr. of Cardiazol and 4 gr. of quinine valerianate. Catarrhal symptoms and infectious diseases, disorders associated with high temperatures and circulatory disturbances, disordered cardiac conductivity.

**Phrenazol (Boots, Nottingham).** Leptazol solution available for use as a cardiac and respiratory stimulant in 1 ml. ampoules and ½ oz. bottles (oral use); for the treatment of narcosis 1, 3 and 5 ml. ampoules are issued; for convulsion therapy 3 and 5 ml. ampoules, 25 ml. vials and Phrenazol powder are available.

**Hexazole.** *Syn.* TRIAZOL 156, CYCLOHEXYL-ETHYL-TRIAZOL. (Marketed on the Continent under the Trade Name "AZOMAN.")

It is readily soluble in water and is employed in the form of a 5% solution, intramuscularly or intravenously, in the convulsion treatment of schizophrenia.

Appears to have several advantages over Cardiazol in the convulsion treatment of schizophrenia, the chief being the lessened unpleasantness of the treatment to the patient, the smaller dosage, and the ease with which failure to induce a fit can be rectified by a supplementary dose, the elimination of venous sclerosis and the possibility of intramuscular use where intravenous injections are impracticable. Convulsions can be readily induced with quantities ranging from 0.7 to 2.5 ml. of 5% solution intravenously, most patients requiring between 1.2 and 1.8 ml. Intramuscularly, approximately twice the intravenous dose is required, but patients vary, and it is best to begin with a somewhat smaller dose.—W. Mayer-Gross and A. Walk, *Lancet*, i/1938, 1324.

A reliable convulsant for both intravenous and intramuscular use, a series of fits having been successfully induced in all the cases tried. It is without danger in cases tried. There is a danger of awakening latent pulmonary tuberculosis.—I. Atkin, *Lancet*, 1/1939, 435.

**Nikethamidum** (*B.P. Add. III*). *Syn. and Prop. Names.* N-DIETHYLNICOTINAMIDE, ANACARDONE (*British Drug Houses, London*), CORAMINE (*Ciba, Horsham*), CORVOTONE (*Boots, Nottingham*), NICAMIDE (*Burroughs, Wellcome, London*).  $C_5H_4N \cdot CO \cdot N(C_2H_5)_2 = 178.1$ .

*Dose.*—3 to 8 grains (0.2 to 0.5 g.); 8 to 20 grains (0.5 to 1.25 g.), by intravenous injection as a stimulant.

It is generally supplied ready for use in the form of a 25% solution.

Nikethamide is pyridine- $\beta$ -carboxylic acid diethylamide, prepared by the action of diethylamine upon the acid chloride obtained by treating nicotinic acid with thionyl chloride. It occurs as a colourless or yellowish oily liquid, or crystalline solid; f.p. 22° to 24°.

*Miscible* in all proportions with water; readily soluble in ether and other organic solvents. Aqueous solutions may be sterilised by autoclaving.

A solution of nikethamide may be prepared as follows:—nikethamide 250, lactic acid 70, concentrated spirit (*P. Dan.*) 50, glycerin 50, distilled water 580.

Solutions of nicotinic acid diethylamide in water or dilute acids were found not to have hydrolysed after autoclaving or after a year's standing. The yellow colour of such solutions is not due to decomposition, but to the presence of 3-nitro-5-(3-pyridyl)-pyrazol, a precursor in the synthesis of nicotinic acid diethylamide.—F. Reimers, *Dansk Tidsskr. Farm.*, 1939, 43, 9.

*Uses.* A powerful cardiac and respiratory stimulant for use by the mouth or by injection. Following its administration there is marked stimulation of the depth and frequency of respiration and an increase in the force of cardiac contraction, the action on the heart being mainly through the central nervous system. It has an extremely low toxicity and does not give rise to undesirable reactions.

Nikethamide is indicated in all cases of shock, collapse or circulatory failure, in asphyxia neonatorum, and in poisoning by carbon monoxide, narcotics and barbiturates.

In acute cases it is usually administered subcutaneously or intramuscularly in a dose of 2 to 3 ml. of a 25% solution, repeated if necessary. In cases of severe collapse it is advisable to give it by intravenous, or even intracardiac, injection in doses of from 5 to 15 ml. of the solution, the injection being made very slowly and with short pauses. In order to interrupt or control the depth and duration of basal anaesthesia with bromethol, from 3 to 5 ml. may be injected intravenously, followed immediately by an intramuscular injection of 5 ml., according to the dose of narcotic used.

In chronic and mild conditions it may be usefully employed by the mouth in a dose of 1 or 2 ml., as in respiratory and circulatory embarrassment during and following pneumonia and other acute infections, in neuro-circulatory asthenia (*e.g.*, repeated fainting



attacks and "D.A.H."), and in the after-treatment of coronary thrombosis.

**ALCOHOLIC INTOXICATION.** Thirty cases of drunkenness, ranging from mild to medium intoxication, successfully treated by administration intramuscularly of 1 or 2 small ampoules of Coramine (1.7 ml.); in severe cases a dose as large as 5.5 ml. was used. In all cases sobriety was obtained in 10 to 15 minutes and vomiting often ceased promptly.—*per Practitioner*, ii/1939, 663.

**BARBITURATE POISONING.** The most useful and reliable method of correcting respiratory depression due to the use of barbiturates during anaesthesia. In practice it can almost be guaranteed to make a patient depressed by a barbiturate wake up enough to require restraint to prevent him falling off the table. It does, however, need to be given in sufficient dosage, 5 ml. or more, and direct into the circulation. A number of other drugs, such as Metrazol and Cardiazol are also needed, but they do not appear to be as effective as Coramine.—F. B. Mallinson, *Brit. med. J.*, i/1940, 123.

**HYPERPIESIS.** Coramine has been given intravenously and intramuscularly in doses up to 2 ml. So far as can be measured with the ordinary sphygmomanometer or an oscillogram, no effect whatever is produced on the blood pressure.—H. Dodd, *Lancet*, i/1940, 358.

**Calcio-Coramine (Ciba, London).** Double salt of pyridine- $\beta$ -carbonic acid diethylamide and calcium thiocyanate. Tablets contain 6 gr. *Dose*.—1 or 2 tablets 3 times a day after meals. Cardiac and respiratory stimulant and expectorant in bronchitis, catarrh, broncho-pneumonia, emphysema, etc.

**Cycliton (Roche Products, Welwyn Garden City).** The diethylamide of 3:5-dimethylisoxazol-4-carboxylic acid supplied in 25% solution for oral use, and in tablets containing 0.1 g.; also in 2 ml. ampoules for injection. *Dose*.—1 to 2 ml. of the oral solution or 2 to 5 tablets; or 2 to 6 ml. of the parenteral solution subcutaneously, intramuscularly or intravenously. A respiratory and circulatory stimulant, and as a restorative in acute poisoning or collapse.

**Icoral (Bayer Products, London).** A 5% solution of a mixture of the hydrochlorides of *m*-oxyethyl-diethylaminoethylaminobenzol and *m*-oxy-*n*-phenylpropanolamine, mixed in the ratio of 4 parts of the former to 1 of the latter. A respiratory and cardiac stimulant used with success in barbituric acid poisoning, carbon monoxide poisoning, morphine poisoning and in a case of quinsy with suffocation. Of no value in severe infections with collapse of purely vasomotor type. Injected intravenously with care (except in cases of severely damaged myocardium) in dose of 0.3 ml. repeated in 20 minutes.—H. Frank, *Dtsch. med. Wschr.*, i/1933, 764.

The prompt elevation of the blood pressure is like that produced by a dose of adrenaline; the rise is excessive and the consequent bleeding from an ordinary wound is heavy. It is felt that this medium is too powerful for surgical purposes, especially in elderly people. Such vigorous stimulation is unnecessary. The useful dose is 0.3 to 0.5 ml. The 1 ml. recommended by the manufacturers gives an excessive response.—H. Dodd, *Lancet*, i/1940, 359.

**Oleum Camphoræ Rectificatum (B.P.C.).** *Syn.* WHITE OIL OF CAMPHOR, OLEUM CAMPHORÆ ESSENTIALE, LIGHT OIL OF CAMPHOR.

Consists of the lighter fractions of the oil obtained in the manufacture of natural camphor. It varies in composition according to the extent to which camphor and saffrole are removed. The heavier fractions of the crude oil are used as a source of saffrole and are known as "brown oil of camphor." The rectified oil contains not less than 35% of cineole. It is a colourless or pale yellow liquid, *soluble* 1 in 3 of alcohol, and is used as a mild counter-irritant in rheumatism, and as a parasiticide.

**Moschus (B.P.C., Fr. Cx.).** MUSK.

*Dose*.—5 to 10 grains (0.3 to 0.6 g.).

The sac containing the dried secretion from the preputial follicles of the musk deer, *Moschus moschiferus* (Ungulata).

**Grain musk** (*Moschus in grano*) is the dried granular secretion. A useful nerve stimulant in cases of exhaustion in fevers and blood poisoning. Of value both for nervous excitement or nervous collapse. Is effective in obstinate hicough and infantile convulsions. The odour of musk is due to muskone,  $C_{15}H_{26}O$ . The butyl derivatives of many aromatic hydrocarbons are sold as **artificial musk**, e.g., MUSK AMBRETE is dinitro-*tert*.-butyl-*m*-cresylmethylether,  $C_6H(C_2H_5)(CH_3)(O\cdot CH_3)(NO_2)_2$ .

**Mistura Moschi.** Musk 5 gr., acacia 5 gr., syrup of orange 1 dr., rose water to 1 oz.

**Tinctura Moschi.** *Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml). 1 in 20 of alcohol 50%. A tincture of artificial musk has been used in whooping cough. In cardiac failure of acute pneumonia it has been given alone in cachets or with camphor in pills.

**Sassafras** (*B.P.C.*) is the dried inner bark of the root of *S. varifolium* (Lauraceæ). Is carminative by virtue of its oil content.

**Sassafras Medulla** is the pith from the stem of *S. officinale*. Forms with water a demulcent mucilage which has been used in eye lotions.

**Sassafras Radix** is the root of *S. officinale*. Contains about 2% of volatile oil.

**Sassafras Cortex** (*P. Helv. V*). The cleaned and dried bark of the root of *S. officinale*. It is used in making compound liquid extract of sarsaparilla.

**Safrolum** (*B.P.C.*). *Syn.* SAFROL, SAFROLE, ALLYL CATECHOL METHYLENE ETHER.  $C_6H_5\cdot C_3H_5\cdot O\cdot OCH_2 = 162\cdot 1$ .

Is the chief constituent of oil of sassafras but is obtained from essential oil of camphor. Occurs as a colourless or yellowish oil with odour of sassafras. Is used for lice and nits in pediculosis. In treating ringworm, the hair is cut close to identify the patches, and the oil applied twice a day by a brush, treatment being continuous for a few weeks if necessary. Non-irritating, pleasant to use, prevents spread of infection and destroys the fungus. Safrole is used also as a perfume for cheap soap, in the manufacture of heliotropin, and is occasionally added to anodyne liniments for rheumatism.

**Oleum Sassafras** (*B.P.C., U.S.P. XI, Fr. Cx.*).

*Dose.*—1 to 5 minims (0.06 to 0.3 ml.). *U.S.P. XI* average dose  $1\frac{1}{2}$  minims.

A pale yellow or reddish oil containing about 80% of safrole. Is used to destroy pediculi, being applied to the hair with a stiff brush.

As an insecticide for dogs and cats safrol, or oil of sassafras, may be extremely toxic in some cases.

## CANNABIS

*B.P.C.*

*Syn.* CANNABIS INDICA (*U.S.P. XI, F.E. VIII, P. Belg. IV, Fr. Cx., P. Helv. V*), MARIHUANA.

[D] "*Indian hemp and resins obtained from Indian hemp and all preparations (except extract and tincture of Indian hemp) of which such resins form the base.*" (See p. 1143.)

"*Any extract or tincture of Indian hemp.*"

[P1] "*Cannabis* (the dried flowering or fruiting tops of *Cannabis sativa* Linn.); the resin of *cannabis*; extracts of *cannabis*; tinctures of *cannabis*; *cannabin* tannate."

[B1] "*Cannabis*; the resin of *cannabis*; extracts of *cannabis*; tinctures of *cannabis*; *cannabin* tannate."

Rule 10 of the Poisons Rules, 1935, exempts from the application of the Pharmacy and Poisons Act, 1933, and of the Rules made under that Act all corn paints in which the only poison is a poison included in the Poisons List under the heading of "*Cannabis*."

Under the "Marihuana Tax Act, 1937," patterned after the Harrison Narcotic Act, the U.S. government extends federal jurisdiction over cannabis so as to cover its intra-state production, manufacture, distribution and use. The real object of the Act is not the raising of revenue but the prevention of the cannabis habit. Under the act, practitioners, dentists and veterinary surgeons who wish to dispense or prescribe cannabis or any of its derivatives or preparations, must register themselves and pay a yearly tax of one dollar. Persons convicted of a violation of any of the provisions of the Act are liable to a fine of not more than 2000 dollars or imprisonment for not more than five years, or both.—*J. Amer. med. Ass.* (Organisation Section), ii/1937, 31B.

The dried flowering or fruiting tops of the pistillate plant of *Cannabis sativa* (Urticacæ). The B.P. '14 required the drug to be obtained from plants grown in India, but this requirement is not included in the B.P.C., since African, American and German varieties are also pharmacologically active.

The masses obtained in European commerce are called Guaza. Ganja differs slightly and is more active. Bhang or Hashish consists of the leaves, small stalks and fruits.

The therapeutic value of the drug is contained in the resin (cannabinone) which contains cannabinol,  $C_{21}H_{26}O_2$ . The latter becomes oxidised on exposure to the air and less active, but even long storage of whole cannabis does not destroy its activity.

Bhang consists of specially dried leaves and flowering shoots of both male and female plants, wild or cultivated. Ganja consists of dried flowering tops of the cultivated hemp-plant which become coated with a resinous exudation. Charas is the name given to the resinous matter collected from the leaves and flowering tops of the plant, and constitutes the active principle of hemp; the best quality and the maximum amount of resin is obtained from plants grown in Yarkand in Chinese Turkestan, and the major part of the charas produced in Chinese Turkestan finds its way into India and forms, indeed, one of the most important articles of trade between Central Asia and India.

The physiological activity of the hemp-plant varies with the locality in which it is grown. The minimum fatal dose by the mouth of charas, ganja and bhang works out at 2000 mg., 8000 mg. and 10,000 mg. per kilo bodyweight respectively.—R. N. Chopra and G. S. Chopra, "The present position of hemp-drug addiction in India," *Indian med. Res. Mem.*, No. 31, July 1939, 1-119.

**Antidotes.** Empty stomach by emetic or stomach tube. Stimulants such as strong black coffee frequently. Strychnine,  $\frac{1}{2}$  gr., hypodermically. Keep patient warm. Artificial respiration may be necessary.

A case of cannabis indica intoxication from the smoking of cigarettes made from the dried leaves and tops of plants grown in England.—E. T. Baker-Bates, *Lancet*, i/1935, 811. See also W. A. J. Fleming, *ibid.*, 1301.

Addiction among marihuana users is unlike addiction among the users of morphine or heroin. With these latter the victim must have the drug to feel normal, but with marihuana the addict wants to recapture the pleasurable euphoric state into which the drug lifts him. It is more of a psychological condition—there is no marked physiological disturbance on withdrawal of the drug.

After long usage, however, a dull state supervenes in which the victim is for all practical purposes an addict, and in which ethical and intellectual deterioration and apathy are the outstanding factors.—W. Bromberg, *Med. Rec.*, ii/1935, 309.

The smoking of marihuana cigarettes has spread from the U.S.A. to Canada, and 34 out of 46 States have promulgated laws to suppress illicit traffic. In New York during 1935 no less than 185 tons of *Cannabis* were destroyed.—E. W. Adams, *Bull. Hyg.*, 1937, 241.

Marihuana: a psychiatric study.—N. Bromberg, *J. Amer. med. Ass.*, ii/1939, 4.

**Uses.** For chordee and asthma, also as an aphrodisiac, and is successful in migraine. Is a narcotic and anodyne, but may give peculiar dreams and even delirium.

It is useful in dysmenorrhœa, especially with gelsemium, and with nux vomica in incipient delirium tremens, nausea, and paroxysmal colic, supraorbital neuralgia, cough of phthisis and for whooping cough. It is of great use combined with chloral in chorea, mental worry and restlessness. Should be given in small and frequent doses. It has been used in menorrhagia.

In gonorrhœa (acute anterior urethritis) cannabis internally with hyosciamus is useful before patient is in condition for injections.

Absorption is greatly facilitated if the drug is taken one hour before a meal, when its action is felt within two hours of administration. If taken after a meal no result may be apparent for as long as six hours.

**HEADACHE DUE TO HIGH BLOOD PRESSURE** well treated, especially where chronic interstitial nephritis is a contraindication to blue pill.—A. Feiling, *Brit. med. J.*, ii/1930, 907.

**HERPES ZOSTER.** Administration of the extract in pill form,  $\frac{1}{4}$  to  $\frac{1}{2}$  grain, according to age, three times a day, quickly relieves the pains.—C. E. Matthews, *Brit. med. J.*, ii/1939, 431.

**[D-P1-81] Extractum Cannabis (B.P.C.).** *Syn.* EXTRACT DE CHANVRE INDIAN (*Fr. Cx.*).

**Dose.**— $\frac{1}{4}$  to 1 grain (0.016 to 0.06 g.), in pill with lycopodium. A soft alcoholic extract.

**[D-P1-81] Extractum Cannabis (U.S.P. XI).** *Average dose.*— $\frac{1}{4}$  grain (0.015 g.). A soft or pilular extract.

**[P1-81] Mistura Cannabis Indicæ (C.H.W.).**

Tincture of cannabis 10 m., spirit of nitrous ether 30 m., solution of ammonium acetate 1 dr., mucilage q.s., camphor water to 1 oz.

**[P1-81] Cannabinæ Tannas.**

**Dose.**—4 to 8 grains (0.25 to 0.5 g.) taken an hour before bedtime in a pill or in sal volatile and water.

A brownish powder, soluble in alkaline water and alcohol, said to be a useful hypnotic and is specially valuable in nervous sleeplessness and in acute mania; also for dysmenorrhœa and menorrhagia.

**Cannabinone** has been used as a hypnotic in doses of  $\frac{1}{4}$  to 1 grain (0.016 to 0.06 g.).

**[D-P1-81] Tinctura Cannabis (B.P.C.).**

**Dose.**—5 to 15 minims (0.3 to 1 ml.). 1 of extract in alcohol 90% to 20. When dispensed in mixtures, mucilage must be added to suspend the resin.

**[D-P1-81] Tinctura Cannabis Indicæ (Fr. Cx.).**

**Dose.**—Maximum single dose 0.5 g., maximum in 24 hours 1 g. 1 in 10, made with alcohol 90%.

[P1-81] *Cannabis Sativa* (P. Helv. V). Russian hemp-seed, oil-free, has been used in form of decoction, strength 100 g. in 1 litre, heated gently and evaporated (without boiling) to 250 ml. 35 to 50 ml. of the resulting liquor is given to children in food.

[D-P1-81] *Fluidextractum Cannabis* (U.S.P. XI).

Average dose.— $1\frac{1}{2}$  minims (0.1 ml.). 1 ml. represents 1 g. of the herb.

**Apocynum** (B.P.C.). Syn. AMERICAN INDIAN HEMP ROOT, CANADIAN HEMP.

Dose.—1 to 5 grains (0.06 to 0.3 g.). U.S.P. VIII average dose 15 grains. The rhizome and roots of *Apocynum cannabinum* and other species of *Apocynum* (Apocynaceæ).

Stated to be a rapid and efficient cardiac stimulant, also an active non-cumulative diuretic, occupying a place between digitalis and caffeine, and has been employed in cardiac dropsy and Bright's disease. It has an irritant action on the stomach, however, and should not be prescribed in acute conditions or in the presence of inflammation of the stomach or intestines.

It is also a powerful emetic, diaphoretic, cathartic and anthelmintic.

Apocynum rhizome varies enormously. It had a great reputation among the aborigines and early settlers for dropsy. Good apocynum is many times more active than digitalis as a heart stimulant.—H. H. Rusby, *Pharm. J.*, ii/1929, 312.

**Decoctum Apocyni.** Dose.— $\frac{1}{2}$  to 1 ounce. 1 in 60.

**Tinctura Apocyni** (B.P.C.). Dose.—5 to 10 minims (0.3 to 0.6 ml.); up to 1 fl. drachm (4 ml.) is sometimes given. 1 in 10 of alcohol 80%. Resembles tincture of digitalis in action but is more irritant. Is used as a diuretic in cardiac dropsy. Large doses may cause gastric ulcerations.

Uremia is warded off by the profuse diuresis it produces and it is of use in removing pleuritic effusion.

**Asclepias incarnata.** Syn. WHITE INDIAN HEMP RHIZOME. Is a speedy, potent and reliable diuretic. Tincture, 1 in 10. Dose.—5 to 40 minims.

**Asclepias tuberosa.** Syn. PLEURISY ROOT. Is expectorant and diuretic. Tincture, 1 in 10. Dose.—5 to 40 minims.

## CANTHARIS

B.P.C., U.S.P. XI, Fr. Cx., P. Helv. V.

Syn. LYTIA, SPANISH OR BLISTERING FLY.

[P1] "Cantharidin; cantharidates."

[81] "Cantharidin except substances containing less than 0.01 per cent. of cantharidin."

"Cantharidates except substances containing less than the equivalent of 0.01 per cent. of cantharidin."

By Rule 10 of the Poisons Rules, 1935, machine-spread plasters are exempt from the provisions applying solely to substances in the First Schedule to the Rules.

Dose.— $\frac{1}{16}$  to  $\frac{1}{2}$  grain (0.004 to 0.03 g.) in pill. Better given as tincture.

The dried beetle *Cantharis vesicatoria*, found in Southern Europe. It contains about 0.4 to 0.8% of cantharidin. P. Jap. V has *Epicauta Gorhami* with 1% of cantharidin.

Cantharides in powder is adjusted to contain not less than 0.6% of cantharidin.

**Antidotes.** Empty stomach by emetics or stomach tube. Medicinal charcoal, stirred up with a dose of magnesium sulphate, has been recommended. Give demulcent drinks freely, but *not* oils or fats. Morphine,  $\frac{1}{2}$  gr., hypodermically for pain. Hot baths or hot applications to the abdomen may relieve the pain.

**Uses.** Externally vesicant, irritant and powerful counter-irritant. Used in pleurisy, pericarditis, meningitis, neuritis, applied above the stomach to stop vomiting, and in rheumatoid arthritis (v. Emplastrum).

Internally is said to have aphrodisiac properties, but its use is inadvisable owing to its irritant action on the gastro-intestinal tract. In cardiac dropsy, cantharides has been used to promote diuresis.

[P1-81] **Ceratum Cantharidis** (U.S.P. XI).

Macerate cantharides 35 parts with a mixture of glacial acetic acid and turpentine, add to a melted mixture of beeswax, resin and benzoinated lard and heat to produce 1000 parts.

[P1-81] **Emplastrum Cantharidis** (U.S.P. XI).

Cantharides cerate 0.1 g. per sq. cm. of adhesive plaster, muslin, paper, or other suitable backing material.

[P1-81] **Tinctura Cantharidis** (U.S.P. XI).

*Average dose.*— $1\frac{1}{2}$  minims (0.1 ml.).

Cantharides 10, glacial acetic acid 10, in alcohol to 100.

[P1-81] **Tinctura Cantharidis** (Fr. Cx.) is made by percolation with alcohol 70%, and contains 0.04% of cantharidin. *P. Ital. V* is similar.

Tincture of cantharides may be prepared by percolation, using as menstruum 3% lactic acid in ethyl alcohol; an improved method.—L. M. Omhart and E. T. Morgan, *J. Amer. pharm. Ass.*, 1939, 385.

[P1-81] **Mylabris** (B.P.C.). *Syn.* CHINESE CANTHARIDES.

The dried beetles *M. Sida* and other species, some of which (e.g., *M. pustulata*) may contain up to 2.3% of cantharidin. It is used as a source of cantharidin and as a substitute for cantharides in India and the East.

[P1-81] **Cantharidinum** (B.P., Fr. Cx., P. Ital. V, P. Helv. V, F.E. VIII, P. Belg. IV).  $C_8H_{12}O(CO)_2O = 196.1$ .

*Dose.*—No dose is given in B.P. '32. Fr. Cx. and P. Helv. V have max. single and max. daily dose 0.0002 g.

Cantharidin is the lactone of cantharidic acid, in flat glistening rectangular prisms, melting at  $216^\circ$  to  $218^\circ$  and volatilising in very irritating white fumes. **Soluble** 1 in 55 of chloroform, 1 in 34 of ether, 1 in 40 of acetone, 1 in about 1100 of alcohol 90%, and about 1 in 150 of ethyl acetate. Soluble also in ether, benzene, glacial acetic acid and fixed oils. Very sparingly soluble in water.

*Poisoning Effects and Antidotes*, see *Cantharis*.

**Uses.** Solutions of cantharidin, as well as other preparations of cantharides, are employed for stimulating the growth of the hair in alopecia, and preventing its falling off.

[P1-81] **Acetum Cantharidini** (B.P.C.) contains cantharidin 1 in an acetic acid solution q.s. to 2000.

[P1-81] **Acetum Cantharidis** (B.P.C.). Cantharis, 1 in 10, extracted by percolation with an acetic acid menstruum.

[P1-81] **Colloodium Vesicans** (B.P.C.) is a coloured solution of pyroxylin in blistering liquid.

[P1-81] **Emplastrum Cantharidini** (B.P.). *Syn.* BLISTERING PLASTER.

Contains cantharidin 0.2% in a basis of beeswax, castor oil and wool fat.

[P1-81] **Emplastrum Calefaciens** (B.P.C.) contains 1 in 5000 of cantharidin.

[P1-81] **Emplâtre Mouches de Milan**, used in France, is similar.

[P1-81] **Emplastrum Lyttæ** (B.P.C.). Powdered cantharides, 1 in 3, in a soft plaster basis. The machine spread plaster is usually prepared with not less than  $3\frac{1}{2}$  ounces of the mass per yard of bleached unglazed calico.

[P1-81] **Linimentum Crinale** (Squire).

Cantharidin 1 gr., ethyl acetate 6 dr.; dissolve with gentle heat, and add alcohol (90%) 6 oz., castor oil 2 oz., lavender oil 15 m. It is better to dilute this with an equal quantity of spirit, and the head should be washed after applying it a few times, to prevent the cantharidin accumulating.

[P1-81] **Liquor Cantharidini** (B.P.C.). *Syn.* TINCTURA CANTHARIDINI. 1 in 10,000; is  $\frac{1}{8}$  strength of *I.A.* *Dose.*—2 to 5 minims (0.12 to 0.3 ml.).

[P1-81] **Liquor Epispasticus** (B.P.) contains cantharidin, 0.4% w/v, with castor oil and colophony in acetone. Should not be applied over too large a surface or toxic effects may occur from absorption.

[P1-81] **Lotio Cantharidini** (B.P.C.). *Syn.* LOTIO CRINALIS STIMULANS. Cantharidin 1 in 5000 with acetone, castor oil and alcohol 90% (or methylated spirit).

[P1-81] **Unguentum Cantharidini** (B.P.C.).

Contains cantharidin 1, dissolved by means of chloroform in benzoinated lard 3000.

One part diluted further with two of soft paraffin forms a useful pomade for stimulating growth of the hair.

[P1-81] **Unguentum Cantharidini Compositum** (W.H.). Vinegar of cantharidin 1 dr., wool fat 30 gr., red mercuric oxide ointment 1 oz.

[P1-81] **Potassii Cantharidas.**

$C_{12}H_{11}O(COOK)_2 \cdot 2H_2O = 326.3$ .

*Dose.*— $\frac{1}{100}$  to  $\frac{1}{500}$  grain (0.00015 to 0.0003 g.) hypodermically in very dilute solution. In minute white needles, soluble 1 in 25 of water. Has properties representative of cantharidin, q.v.

## CAOUTCHOUC

*B.P.C., Fr. Cx., P. Helv. V.*

**India-Rubber.** *Syn.* ELASTICA, CAUTSCHUC (*P. Jap. V.*).

The prepared milk-juice of *Hevea brasiliensis* (Euphorbiacæ) and other species; known in commerce as pure Pará rubber.

**Preservation.** The best means of preserving rubber goods is to immerse completely in distilled water.

**Bandages of rubber:**—(i) Webbed with strands of rubber; (ii) Statham's porous; (iii) Martin's (solid) perforated and non-perforated; (iv) elastic circular stockings and india-rubber webbing.

**Bougies of solid elastic gum:**—

With bulbous end = a Boule, in sizes 1 to 16.

" " silk web " " 1 to 16.

Conical pointed in shape " " 1 to 12.

Cylindrical, not tapered, various textures and materials—sizes 1 to 16.

(Esophageal bougies are bulbous, conical and cylindrical, of elastic gum.—Sizes 10 to 24.)

**Catheters.** Elastic gum, black and webbed, or silk web:—

Bulbous (a Boule).—Sizes 1 to 16.

Coudé (bent at end) also Bi-Coudé with two bends.—Sizes 5 to 12.

Cylindrical.—Sizes 1 to 15, with or without wire stilettes, and sizes 5 to 12 with solid or hollow ends.

Conical (simply pointed, *i.e.*, tapered), with wire stilette.—Sizes 1 to 12.

**Catheters, Soft Rubber.**—13 and 16 inches long, with and without funnels, and the sizes vary between 4 and 12.

Self-staining catheters are also prepared.

Web catheters may be sterilised by boiling in nearly saturated solutions of ammonium sulphate or sodium chloride, washing afterwards in sterile water.

**Catheters, Female,** are of glass, straight or curved, metal, or soft rubber.

**Dental Rubber,** manufactured of pure Pará rubber and coloured. This is supplied in various shades of colour, *e.g.*, white, pink, red, orange, black. The varieties in commerce are designated "Samson," "Doherty," "Gold Dust," Ash's "Whalebone," and Jamieson's "Horn." The rubber is hardened by vulcanisation and used to form a frame to carry artificial teeth. In vulcanising most rubber, especially Ash's, raise the temperature gradually until 315°F. or 100 lbs. pressure is obtained. Maintain this temperature or pressure 75 minutes to complete vulcanising process.

**Mackintosh or Waterproof Sheeting,** 36 and 54 inches wide is supplied having rubber on one or both sides.

**Stomach Tubes.** That known as Van Valsh's, with bevelled "Velvet Eyes," is considered one of the best, but the bevelling may have the disadvantage of weakening the tube on one side and causing it to turn round when an obstruction is met. For passing the tube a special lubricant jelly is supplied, or a glyco-gelatin pastille of menthol and cocaine is useful.

**Emplastrum Adhesivum (B.P.C.)** is spread with a rubber adhesive compound containing not more than 25% of fillers.

**Elastic Adhesive Bandages.** Elastic adhesive bandages are self-adhesive, resilient bandages consisting of elastic cotton fabric spread with a rubber adhesive compound, and available in various widths and lengths. They are usually medicated with zinc oxide.

**Uses.** These bandages have been much used as a tight binder for varicose veins and ulcers, both for support and for fixing zinc gelatin dressings. They also provide compression and support for the after-treatment of fractures and dislocations, etc. X-ray photographs can be taken through several layers of them. Elastic adhesive bandages have also been used in the treatment of bed-sores, boils and impetigo, the bandage being applied to the affected area, left on for a period of from four to six days and then changed.

**VARICOSE ULCERS.** The standard practice is the ambulatory treatment by the Dickson-Wright method (*see Brit. med. J.*, ii/1930, 996), using elastic adhesive bandages. A broad strip of bandage is placed longitudinally along the whole length of the inside and outside of the leg. Commencing at the toes, a bandage



is then wound firmly around the limb in an ascending spiral, each succeeding loop overlapping the preceding one by about two-thirds of its width. It is essential that the bandage is applied firmly. The limb is thus totally encased in a supportive material which will allow standing or walking.

**BOILS.** Twenty cases successfully treated by the occlusive method. The dressing used was Elastoplast bandage applied directly to the shaven skin and extending well beyond the outer limit of the inflamed area, the surrounding skin being sterilised with 1:1000 acriflavine solution. The average number of dressings was 2 or 3 and the average days under treatment 11 or 12.—P. K. Fraser, *Brit. med. J.*, ii/1935, 894.

**IMPETIGO.** Treatment by occlusive dressing consisting in the application of a piece of Elastoplast bandage to the lesion without cleaning adjacent skin, removing crusts or pricking pustules, and leaving the bandage in situ. Total time lost by school children 9.7 days per child, compared with 18.6 days by Ung. Hyd. Ammon. Dil. treatment and 22.5 days by intensive ointment treatment and removal of crusts by starch poultices. Results better and infectivity of the disease diminished.—J. L. Newman, *Brit. med. J.*, i/1933, 823. Confirmation.—J. M. Morris, *ibid.*, 986.

**VARICOSE ULCERS.** Reflux pressure in the veins may upset the hydraulics on removing bandage. Single long veins easiest to treat.—F. A. E. Silcock, *Brit. med. J.*, i/1931, 34.

Varicose ulceration. Compression or squeezing of excess fluids out of the limb. Very tight bandaging required.—J. H. Twiston Davies, *Brit. med. J.*, i/1931, 201.

Support is given which skin and tissues have lost and the blood is made to circulate properly. Patients should walk about.—Sir L. Hill, *Brit. med. J.*, i/1931, 240.

Painting the leg with 5% ichthylol in glycerin prevents irritation.—R. W. Cockshut, *Brit. med. J.*, i/1931, 652.

If there is the slightest concurrent varicose eczema present, as is often the case, along with varicose ulceration, then the application of elastic, adhesive, and occlusive bandages, is absolutely asking for trouble in the form of further skin disorder. The use of Unna's Zinc-Gelatin bandage is still one of the best methods of treating varicose ulcers.—F. A. E. Silcock, *Brit. med. J.*, ii/1939, 1205.

Although it is true that adhesive elastic bandage has an irritating effect on some skins, it is the sheet anchor of the treatment of varicose ulcer, just as the organic preparations of arsenic are the mainstay of the syphilologist, even though they occasionally cause arsenical poisoning.—H. Haldin-Davis, *Brit. med. J.*, i/1940, 231.

**WARTS.** A simple and effective treatment for warts on the hands is to bind the warty parts tightly with Elastoplast, which is removed once a week, the softened epithelial debris being scraped away with a blunt scalpel.—McAusland, *Brit. med. J.*, i/1935, 1123.

**Ligamentum Elasticum Adhesivum (B.P.C.)** is spread with rubber adhesive plaster containing not less than 20% of zinc oxide.

**Elastoplast Bandages** (T. J. Smith & Nephew, Hull). Elastic adhesive bandages medicated with zinc oxide.

**Semiplast Bandages** (T. J. Smith & Nephew, Hull) are elastic adhesive bandages spread only half-way across with adhesive rubber base.

**Viscopaste Bandages** (T. J. Smith & Nephew, Hull). Elastic adhesive bandages spread with gelatin.

**Variban Bandages** (Cuxson, Gerrard, Birmingham). Elastic adhesive bandages impregnated with zinc oxide.

**Ceraban Bandages** (Cuxson, Gerrard, Birmingham). Adhesive elastic, porous roll bandages spread with a lead-base plaster and free from rubber and gum.

**Crepoplast** (Herts Pharmaceuticals, Welwyn Garden City), **Dalzoflex** (A. De St. Dalmaz, Leicester), **Elastikon** (Johnson & Johnson, Slough), and **Vitaplast** (Carnegie Bros., London), are also elastic adhesive bandages.

**Liquor Caoutchouc** (B.P. '98). Caoutchouc 1, benzene 10, carbon disulphide 10. Treat the rubber with the carbon disulphide for an hour or two to form a jelly, and add the benzene. It may be medicated, but traumaticin is preferable.

**Gutta Percha** (B.P.C., *Fr. Cx.*).

The dried purified latex of *Palaequium oblongifolium* and other species (Sapotaceæ). Occurs in lumps, brownish externally, reddish-yellow or reddish-grey internally, and consists chiefly of the hydrocarbon gutta, ( $C_8H_8$ )<sub>n</sub>.

The principal districts of supply are Pahang, Kelantan, Siak, Bolungen and Sarawak. Small quantities are also exported from Siam and Manila, and a lower grade from Nigeria. From Borneo is obtained the well-known "leaf gutta"; this is extracted from the leaves and small twigs of the tree, and is boiled, cleaned, and pressed into slabs and cakes, considered by some to be the best. Unfortunately on keeping it oxidises and becomes brittle.—*Chem. & Drugg. Commercial Compendium*.

[P1] **Liquor Gutta Percha** (B.P.C.). *Syn.* TRAUMATICIN. Gutta percha 10% w/v in chloroform. *P. Belg.*, *P. Ital. V*, *F.E. VIII*, *P. Jap. V* and *P. Ned. V* use gutta percha (purified) 1, chloroform (by weight) 9. More cleanly than liniments or ointments.

**Tela Gutta Percha** (B.P.C.). Gutta percha tissue is gutta percha in thin sheets.

**Sericum** (B.P.C.). Silk.

The prepared fibre from the cocoons of the silkworm, species of *Bombyx* and of *Antheraea*. The fibre is unwound from the cocoons and degummed. The threads are solid and rounded or rounded-triangular in cross-section. They are soluble in 5% aqueous potassium hydroxide.

**Sericum Oleatum** (B.P.C.). Oiled Silk.

A silk fabric made waterproof by treatment with a drying oil, often coloured with a green dye.

**Sindon Oleata** (B.P.C.). Oiled Cambric. *Syn.* YELLOW OILED CAMBRIC.

A bleached cotton cloth made waterproof by treatment with a drying oil.

## CAPSICUM

(with ARNICA, PIPER, ETC.)

B.P., U.S.P. XI.

*Syn.* CAYENNE, AFRICAN PEPPER, CHILLIES, CAPSICI FRUCTUS.

*Dose.*— $\frac{1}{2}$  to 2 grains (0.03 to 0.12 g.), in a pill.

The dried ripe fruit of *Capsicum minimum* (Solanaceæ) (*C. frutescens*). Capsicum (*P. Helv. V*, *P. Dan.*) is from *C. annum* var. *longum*.

Contains as chief constituent capsaicin,  $C_{18}H_{27}O_3N$ , the average content being about 0.14%.

*Uses.* Internally, capsicum has a tonic and carminative action, especially of value in atonic dyspepsia, but contraindicated in gastric catarrh. Externally, it is employed as a counter-irritant in lumbago, neuralgia and rheumatic disorders.

**Emplastrum Capsici** (B.P.C.). Contains 1 in 50 of oleoresin of capsicum in plaster of colophony.

**Emplastrum Capsici Elasticum** (*B.P.C.*) is the same strength as the preceding but is made with rubber adhesive plaster. The machine spread plaster is usually prepared with about 4 ounces of mass per square yard, on bleached cotton cloth of plain weave.

**Emplastrum Capsici Mitis** (*R.D.H.*).

Caoutchouc 10, yellow soft paraffin 1; heat carefully so as just to liquefy and add colophony 10, orris 4, capsicum, finely powdered, 4. Spread thinly on holland or linen and cut into pieces half the size of a finger-nail.

**Emplastrum Capsici Fortis** (*R.D.H.*).

Prepare as above, omitting the capsicum. When spread, brush the surface with a thin coating of compound capsicum ointment (*B.P.C.*).

These plasters are for dental use.

**Fluidextractum Capsici.**

*Dose.*—1 minim (0.06 ml.). Alcoholic percolate, 1 = 1. Gerrard advised the following formula:—

Exhaust capsicum 100 with 90% alcohol, distil off alcohol until the residual extract weighs 50; 1 of extract = 2 of drug.

**Gossypium Capsici** (*B.P.C.*). *Syn.* CAPSICUM WOOL, CALORIFIC WOOL. Contains the equivalent of about 20% of capsicum.

Alternative formula (Gerrard):—

Dissolve liquid extract of capsicum (Gerrard) 2 oz. in alcohol 90% 7 oz. Pour the solution on to the cotton wool 9 oz. under pressure to saturate evenly. Dry and preserve in well closed cartons. Contains 10% extract. Colour with eosin, as otherwise the colour fades. Cover with oiled silk when applying, to increase activity.

**Linimentum Capsici** (*B.P.C.*).

Stronger tincture of capsicum about 1 in 3, with oleic acid, oil of lavender and alcohol.

Painted on the skin, or applied sprinkled on piline or flannel, it produces a red glow within one hour; its action may be arrested by smearing the part with soft paraffin. Useful in chest affections, rheumatism, sciatica, etc. Does not redden the skin for any length of time, hence may be used on exposed parts.

**Mistura Capsici Sedativa** (*L.H.*).

Potassium bromide 10 gr., sodium bicarbonate 10 gr., tincture of capsicum 5 m., strong tincture of ginger 5 m., infusion of quassia to  $\frac{1}{2}$  oz. For alcoholic dyspepsia.

**Oleoresina Capsici** (*B.P.C.*). *Syn.* CAPSICIN.

*Dose.*— $\frac{1}{100}$  to  $\frac{3}{50}$  grain (0.0006 to 0.002 g.).

Made by extracting with ether, and evaporating the solvent, extracting the residue with alcohol 90% and removing the alcohol by evaporation. It is approximately four times as strong as the oleoresin of the *B.P.C.* 1923, and occurs as a dull reddish-brown oily mass becoming crystalline.

Commercially, so-called oleoresins are also available, consisting of the extractive obtained by percolation with ether or with acetone.

**Pigment. Capsici c. Methyl. Sal.** (*N.I.F.*).

Oleoresin of capsicum 3 gr., rectified oil of turpentine 2 dr., methyl salicylate 1 dr., rectified oil of camphor to 1 oz.

**Pŭla Capsici Composita.**

Capsicum oleoresin  $\frac{1}{2}$  m., clove oil  $\frac{1}{2}$  m., calomel 1 gr., aloe  $\frac{1}{2}$  gr. For the atonic stomach of drunkards.

The proportion of oleoresin should be reduced owing to the increased strength of the B.P.C. 1934 preparation.

**Tela Carbasi et Gossypii Capsici (B.P.C.).** *Prop. Names.* THERMOGENE (*Veno Drug Co., Manchester*), CAPSOGEN (*Southall Bros. & Barclay, Birmingham*). Capsicum tissue consists of capsicum wool enclosed in absorbent gauze.

**Tinctura Capsici (B.P.).**

*Dose.*—5 to 15 minims (0.3 to 1 ml.).

1 in 20 of 60% alcohol.

Given internally it increases the flow of saliva and gastric juice. Increases peristalsis, relieves atonic dyspepsia, and is useful in dipsomania—it allays the craving for alcohol (*cf.* Mistura Capsici Sedativa). The B.P. tincture is too weak for external use as a counter-irritant.

**Tinctura Capsici (U.S.P. XI).** *Average dose.*—8 minims (0.5 ml.). 1 in 10.

**Tinctura Capsici Ætherea.**

Prepared as B.P. tincture, with ether instead of alcohol.

**Tinctura Capsici Fortior (B.P.C.).** *Syn.* TURNBULL'S TINCTURE OF CAPSICUM.

*Dose.*—1 to 3 minims (0.06 to 0.2 ml.). 1 in 3. Principally used externally. Is useful for chilblains, but only when the skin is not broken. This is too irritating generally.

**Unguentum Capsici (B.P.).**

Capsicum, bruised, 25% in a basis of soft and hard paraffins and lard, strained after digesting an hour on the water bath.

*B.P. Add. II* authorises the use of simple ointment, prepared with yellow soft paraffin, in place of lard and hard and soft paraffins, in making capsicum ointment.

[P1] **Unguentum Capsici Compositum (B.P.C.).** *Syn.* UNGUENTUM OLEORESINÆ CAPSICI COMPOSITUM, CHILLIE PASTE.

Oleoresin of capsicum 2%, with menthol, chloral hydrate and camphor in yellow soft paraffin.

**Unguentum Capsici Forte (B.P.C.).**

Oleoresin of capsicum 4.5% in yellow beeswax and benzoinated lard. May be too strong for tender skins—will bear dilution 2 or 3 times.

**Capsolin (Parke, Davis, London).** Camphor, oleoresin of capsicum, oil of turpentine, oil of cajuput and croton oil in ointment form for use as external counter-irritant to counteract local congestion, muscular rheumatism, neuralgia, etc.

**Arnica Flos (B.P.C., Fr. Cx.).**

The dried flowerheads of *Arnica montana* (Compositæ). Gastric and intestinal irritant. The tincture is employed externally as a local application to sprains and bruises when the skin is unbroken.

**Antidotes.** Give emetic if patient has not already vomited. Medicinal charcoal, stirred up in water, may be given freely, also demulcent drinks.

**Tinctura Arnicae Floris (B.P.C.).** 1 in 10. Local application may produce severe dermatitis. Under saline purges and sedative ointment rash and irritation subside. *Fr. Cx.* has 1 in 6 with alcohol 60%.

**Arnicae Rhizoma** (B.P.C.). *Syn.* ARNICA ROOT.

The dried rhizome and rootlets of *A. montana* (Compositæ).

**Linimentum Arnicae** (B.P.C.). *Syn.* ARNICA OPODELDOC.

A solid liniment containing 1 in 4 of tincture of arnica root in a soap basis.

**Tinctura Arnicae Radicis** (B.P.C.). *Syn.* TINCTURE OF ARNICA. 1 in 20.  
Used externally as a local application for sprains and bruises.

**Calendula** (B.P.C.). *Syn.* MARIGOLD FLOWERS. Dried florets of *Calendula officinalis* (Compositæ).

**Tinctura Calendulae** (B.P.C.). 1 in 5 of alcohol 90%. *Dose.*—5 to 20 minims. Applied to sprains, diluted with 20 to 30 parts of water, and given in amenorrhœa. It has diuretic and stimulant properties.

[P1-81] **Cevadilla** (B.P.C., *Fr. Cx.*, *P. Helv. V*, *P. Dan.*).

*Syn.* SABADILLA, CAUSTIC BARLEY.

[P1] "Alkaloids, the following; their salts, simple or complex:—*Sabadilla, alkaloids of.*"

[81] "Alkaloids, the following; their salts, simple or complex:—*Sabadilla, alkaloids of, except substances containing less than 1% of the alkaloids of sabadilla.*"

[86] "Alkaloids—*sabadilla, alkaloids of—specify proportion as the proportion of any one alkaloid of sabadilla that the preparation would be calculated to contain on the assumption that all the alkaloids of sabadilla in the preparation were that alkaloid.*"

The dried ripe seeds of *Schœnocaulon officinale* (Liliacæ), containing the alkaloid cevadine (*syn.* veratrine, which name has also been given to veratridine, an amorphous alkaloid, and to indefinite mixtures of cevadine and veratridine).

Used as a parasiticide, especially for pediculosis capitis, in the form of [P1-81] ointment 20% or as—

[P1-81] **Acetum Cevadillæ** containing 10 of cevadilla macerated in alcohol 10, acetic acid 17.5 and water to 100.

[P1-81] **Veratrina** (B.P.C., *Fr. Cx.*, *P. Helv. V*, *P. Ned. V*). *Syn.* AMORPHOUS VERATRINE.

*Dose.*—*Fr. Cx.* has max. single dose 0.002 g., max. in 24 hours 0.01 g.

A mixture of alkaloids from cevadilla containing cevadine (crystallised veratrine),  $C_{27}H_{49}O_5N$ , veratridine,  $C_{27}H_{53}O_{11}N$ , cevadilline,  $C_{24}H_{53}O_8N$ , sabadine,  $C_{29}H_{51}O_8N$ , and cevine,  $C_{27}H_{43}O_3N$ . It occurs as a whitish or greyish powder with bitter taste followed by numbness of the tongue. *Soluble* about 1 in 3 of alcohol 90%, 1 in 6 of ether, 1 in 3 of chloroform and in other organic solvents, also in acids, forming salts.

**Antidotes.** If patient has not vomited freely, empty stomach by emetic or stomach tube. Give medicinal charcoal, stirred up in water. Keep patient warm, lying down with head rather lower than the rest of the body. Stimulants, *e.g.*, aromatic spirit of ammonia  $\frac{1}{2}$  dr. in water by mouth, or hot, strong coffee by rectum. Atropine,  $\frac{1}{100}$  gr., hypodermically.

**Uses.** Is applied externally, where the skin is not broken, for its antispasmodic properties in neuralgia, and in the form of an ointment as a parasiticide, especially for pediculosis capitis. It is seldom

employed internally, owing to its violent irritant action on the mucous membranes, even in minute doses.

**Caution.**—Its sternutatory properties are most marked.

[P1-81] *Oleinatum Veratrinæ* (B.P.C.). 2% w/w in oleic acid and olive oil.

[P1-81] *Unguentum Veratrinæ* (B.P.C.). 2% in oleic acid and benzoinated lard.

[P1] **Veratrum Album** (B.P.C., *P. Helv. V*). *Syn.* WHITE HELLEBORE RHIZOME.

[P1] "*Alkaloids, the following; their salts, simple or complex:—Veratrum, alkaloids of.*"

[81] "*Alkaloids, the following; their salts, simple or complex:—Veratrum, alkaloids of, except substances containing less than 1% of the alkaloids of veratrum.*"

[86] "*Alkaloids—veratrum, alkaloids of—specify proportion as the proportion of any one alkaloid of veratrum that the preparation would be calculated to contain on the assumption that all the alkaloids of veratrum in the preparation were that alkaloid.*"

The dried rhizome and roots of *V. album* (Liliaceæ). Contains jervine, protoveratrine and other alkaloids. Formerly used internally as a cardiac depressant and diuretic, and to lower the temperature in the early stages of pneumonia and other acute infections, but is now seldom employed.

[P1] **Veratrum Viride** (B.P.C., *U.S.P. XI*). *Syn.* AMERICAN HELLEBORE, GREEN HELLEBORE RHIZOME.

*Dose.*—*U.S.P. XI* average dose  $1\frac{1}{2}$  grains.

The dried rhizome and roots of *V. viride* (Liliaceæ). Contains various alkaloids as in white hellebore. Is a powerful cardiac, nerve and arterial sedative, useful in puerperal eclampsia, hyperpiesia and in aneurism.

Both the preceding must be distinguished from *Helleborus Niger* (Ranunculaceæ), or Christmas Rose, which is purgative and emmenagogue and has strong sternutatory properties. It is now little used.

*H. niger* and *H. viride*—a comparative study. It is not possible at present to find any character enabling one to distinguish with certainty between these rhizomes and roots.—T. E. Wallis and A. M. Saunders, *Pharm. J.*, ii/1924, 90.

[P1] *Tinctura Veratri* (B.P.C.). *Dose.*—5 to 30 minims (0.3 to 2 ml.). 1 in 10.

[P1] *Tinctura Veratri Viridis* (U.S.P. XI).

*Average dose.*—15 minims (1 ml.). 1 in 10.

[P1] *Veratrone* (Parke, Davis, London). An extract of veratrum 1 ml. of which is equivalent to 20 minims of tincture. In eclampsia.

**Helborsid.** A solution of hellebrin, a crystallised pure glycoside of *Helleborus niger*, is about 20 times more active than helleborein; aqueous solutions are highly stable and retain their efficacy for years. The pharmacologic properties of hellebrin greatly resemble those of strophanthin. It is a highly effective cardiac stimulant. It is less toxic than strophanthin and its secondary effects are either absent or appear later and in a milder form. It is administered intravenously, an initial dose of 0.5 ml. of solution is given (containing 0.25 mg. of hellebrin) and is increased later to 1 ml., the injections being given daily until the desired effect is obtained, and then intermittently. 74 patients with various forms of cardiac decompensation were treated with good results.—M. Grossmann and B. Benzon, *Schweiz. med. Wschr.*, 1940, 70, 251.

**Piper Nigrum** (*B.P.C.*, *P. Jap. V*). *Syn.* PIPER. *Dose.*—5 to 10 grains (0.3 to 0.6 g.).

The dried unripe fruits of *Piper nigrum* (Piperaceæ). Contains 5 to 9% of the alkaloid piperine and 1 to 2.5% of volatile oil.

Black pepper has stimulating, carminative and diuretic properties.

**Piper Album** is black pepper fruits from which the outer coatings have been removed. It contains less volatile oil than black pepper.

**Piper Longum.** *Dose.*—5 to 10 grains (0.3 to 0.6 g.) is the dried unripe fructification of *P. Chaba* (Piperaceæ). Contains about 5% of piperine and 1% of volatile oil.

**Confectio Piperis** (*B.P.C.*). Black pepper 10% with caraway and purified honey.

**Piperina.**  $C_{17}H_{19}O_3N = 285.2$ . *Dose.*—1 to 10 grains. A crystalline principle from the fruits of *Piper nigrum* and *Piper longum* (Piperaceæ). Melts at  $130^\circ$ . Insoluble in water, soluble in alcohol. It has febrifuge, stomachic and antiperiodic action.

**Oleoresina Piperis.** *Average dose.*— $\frac{1}{2}$  grain. Is prepared by acetone extraction of pepper.

**Piperidine.** *Syn.* HEXAHYDROPYRIDINE.  $C_4H_{11}N$ . A colourless liquid with peppery odour and taste; b.p.  $106^\circ$ .

**Piperidinæ Tartras.** *Syn.* PIPERIDINE ACID TARTRATE.

*Dose.*—10 to 15 grains (0.6 to 1 g.).

Colourless pleasant-tasting crystals, readily soluble in water. Uric acid solvent.

**Effervescent Piperidine Tartrate.**

*Dose.*—1 drachm or more; 5 grains in 1 drachm.

**Dolantal** (*Bayer Products, London*). The carboxylic acid ethyl ester of 1-methyl-4-phenylpiperidine, a spasmolytic and analgesic in .25 mg. tablets for oral administration, and ampoules containing 100 mg. in 2 ml. for intramuscular injection. Advocated for spasm of the intestinal tract, urogenital system, etc., and for the relief of pain in carcinoma, arthritis, etc. *Dose.*—1 to 2 tablets or 1 ampoule 3 times daily. The ampoules may be given by slow intravenous injection for prompt relief.

**Piperazina** (*B.P.C.*, *F.E. VIII*). *Syn.* PIPERAZINE HYDRATE (*Fr. Cx.*).

*Dose.*—5 to 15 grains (0.3 to 1 g.).

In colourless, glassy deliquescent tablets, absorbing atmospheric carbon dioxide to give the carbonate, and containing 44% of anhydrous piperazine. M.p. about  $43^\circ$ . M.p. of anhydrous base about  $109^\circ$ .

Very *soluble* in water; soluble 1 in 2 of alcohol; insoluble in ether.

**Incompatible** with alkaloidal salts, iron salts, quinine, sodium salicylate, spirit of nitrous ether.

**Uses.** Given internally for the uric acid diathesis, in gout and rheumatism, and urinary calculi. Said to prevent change from glycogen into sugar in diabetes.

**Piperazina Effervescens** (*B.P.C.*).

*Dose.*—1 to 3 drachms (4 to 12 g.). Contains about 5 grains per drachm.

**Urazine** (*Pharmaceutical Specialities (May & Baker) Ltd., London*). Piperazine citro-salicylate in effervescent granules for use in rheumatism, gout, etc.

## CARBO

*B.P.C., Fr. Cx., P. Jap. V, P. Dan.*

*Syn. CARBO LIGNI, MEDICINAL CHARCOAL.*

*Dose.*—1 to 2 drachms (4 to 8 g.).

Made by burning wood, *e.g.*, willow, with access of as little air as possible.

In cachets or as charcoal biscuits as an adsorbent in distension of the stomach, *e.g.*, in dyspepsia. Is antiseptic, and is used externally as a poultice to foul ulcers.

A test of activity of medicinal and other charcoals by exposure to water and other vapours. Active charcoal will absorb 50 to 100%, or even more, of moisture. The water figure is slightly higher than that for alcohol or turpentine. *Pulv. Carbo. Lig.* as ordinarily dispensed for medicinal purposes is inactive. The author suggests improvements in the manufacture and the adoption in the *B.P.* of tests for activity.—H. Brindle, *Pharm. J.*, ii/1928, 84.

It has been calculated that 15 grains of medicinal charcoal can absorb *in vitro* 13 gr. of corrosive sublimate, 20 gr. of iodine, 9 gr. of strychnine, 4.5 gr. of phenol from 1% solution, 8 gr. of potassium permanganate.—G. H. W. Lucas and V. E. Henderson, *Canad. med. Ass. J.*, ii/1933, 22.

*Cataplasma Carbonis (B.P.C.).* 10% in linseed poultice.

**Carbo Activatus** (*B.P.C., U.S.P. XI, Fr. Cx.*). *Syn. and Prop. Names.* DECOLOURISING CARBON, NORIT (*Norit, Amsterdam; C. Zimmermann, London*), ULTRACARBON (*Merck, Darmstadt; Savory & Moore, London*). CARBOSERIN (*Bayer Products, London*) is activated charcoal in tablet form.

*Dose.*—As for Carbo.

Prepared by heating charcoal to a high temperature in a stream of steam or other activating gas (by which its adsorptive power is greatly increased), washing and drying. *U.S.P. XI* states that Carbo Activatus may be dispensed when Carbo Ligni is prescribed.

Activated charcoal is employed in the containers of "Service" and "Civilian Duty" gas respirators for adsorbing toxic gases.

Activated charcoal adsorbs or inactivates strychnine, brucine, adrenaline, histamine and tyramine. With ephedrine and acetylcholine adsorption or destruction is not quite complete.—F. Saunders and co-workers, *J. Pharmacol.*, June, 1931, 177.

**Carbo Animalis** (*B.P.C.*) is prepared by boiling crude animal charcoal with hydrochloric acid, washing and drying. *P. Helv. V* describes Carbo Adsorbens, Carbo Adsorbens Granulatus and Carbo Ligni; the first must be dispensed when Carbo Animalis is prescribed. *Fr. Cx.* describes ordinary animal charcoal made by burning bones (Carbo Ossium) and purified animal charcoal (Carbo Ossium Acido Depuratus), in addition to Carbo Ligni and Carbo Activatus.

A 2% aqueous suspension has been widely employed, especially on the Continent, by intravenous injection in a variety of infective conditions. There is a possibility of risk, however, in this procedure; death from pulmonary embolism has occurred in rabbits following intravenous injection of from 2 to 5 ml.

Over 100 patients treated, including 14 cases of acute puerperal infection, 5 of pneumonia, 3 of acute cholecystitis, and 5 of furunculosis. No reaction, and all



patients recovered. Initial dose 3 ml. of a 2% suspension of finely pulverised animal charcoal, the piston of the syringe, and the needle, being lubricated with liquid Vaseline to prevent jamming.—E. Saint-Jacques (Montreal), *Lancet*, i/1934, 418.

Doses consist of 2 to 5 ml. of a 1 to 3% suspension of charcoal in isotonic glucose serum, injections being given daily, or every other day, or at longer intervals, the maximum total dosage being 42 ml. of a 2% solution. Injections painless, free from violent or febrile reaction. Best results in diffuse inflammatory processes when reaction of the organism to the infection hangs fire, or when it runs an acute and serious course without free suppuration.—Gaudier and Demarez, *Bull. Acad. méd., Paris*, 1934, 112, 45.

**ERYSIPELAS.** Intravenous injections of 3 to 5 ml. of a 2% suspension of animal charcoal in a 10% hypertonic dextrose solution bring about a rapid process of recovery—the pain and tension stop, the fever abates and then disappears, the erysipelatous patches lose their lustre and regress, general symptoms improve, and desquamation rapidly takes place.—H. D. Gonzalez and M. Scheingart, per *J. Amer. med. Ass.*, i/1936, 1430.

**FEBRILE DISEASES.** Intravenous injections of 4 to 5 ml. of a 2% suspension of charcoal in saline or gum-saline produced no benefit in 123 cases of febrile disease. In afebrile cases an average leucocyte increase of 45% was produced in five hours, but gum-saline alone produced a leucocytosis of 50%. The response to charcoal in several ways resembles the response to injections of proteins and colloids.—E. Davis, *Lancet*, ii/1936, 1266.

**SKIN DISEASES.** 50 severe skin cases were treated with intravenous charcoal injections; promising results were obtained in acute eczema, boils, impetigo, and seborrhæic dermatitis. The dosage recommended for an adult is 4 ml. of a 2% suspension in distilled water or gum-saline (children tolerate charcoal well in doses of 2 to 3 ml.). Each successive dose should be increased by 0.5 ml. and given at intervals of 24 to 48 hours. Charcoal should be continued until recovery seems established, and repeated should there be signs of a relapse, or if recovery becomes sluggish; it is contraindicated in very debilitated patients. A collapse reaction contraindicates further charcoal, and doses of 8 ml. or more should be given with caution, if at all. If four injections have been given without benefit it is unlikely that charcoal will be of use. In afebrile individuals the injections often cause an elevation of pulse, temperature and respiration, which may be associated with chills and rigor.—E. Davis, *Brit. J. Derm.*, 1936, 495.

**Carboacid (Richter, London).** Charcoal containing 2% of HCl. *Dose.*—2 tablets 3 times daily with meals. In flatulent dyspepsia, etc.

**Carbact (Wilcox, Jozeau, London).** Activated charcoal tablets, each containing activated charcoal 3 gr., bismuth tribromphenate  $1\frac{1}{2}$  gr., dried extract of rhubarb  $\frac{1}{2}$  gr., excipient to  $7\frac{1}{2}$  gr. *Dose.*—2 tablets three times a day. Gastro-intestinal disorders, flatulent dyspepsia, gastro-enteritis, etc.

**Carbolax (Richter, London).** Tablets containing activated charcoal 7 gr., with diphenolisatine  $\frac{1}{4}$  gr. *Dose.*—Two tablets three times daily with meals. Habitual constipation.

**Carbonei Dioxidum (B.P., U.S.P. XI).** *Syn.* CARBONIC ANHYDRIDE.  $\text{CO}_2 = 44$ .

Carbon dioxide in the gaseous condition when used in dilutions of 4 to 6% with oxygen stimulates expiration, acts as a cardiac stimulant, exerts an indirect effect as a sedative and tones up a weak pulse. It is employed after an anæsthetic and operation, also in pneumonia and in asphyxia, e.g., from electric shock, carbon monoxide poisoning, and drowning.

**ACUTE ALCOHOLISM.** Acute alcoholic coma with dangerous respiratory depression, paralysis and cyanosis is a medical emergency. Death may be definitely prevented and recovery accelerated by inhalation of a mixture of 10% carbon dioxide in 90% oxygen for a length of time sufficient to maintain normal respiration and colour, even after the inhalation is suspended. A minimum time of half an hour should be observed.—L. J. Robinson and S. Selesnick, *J. Amer. med. Ass.*, ii/1935, 1735.

**ANÆSTHESIA.** Carbon dioxide and oxygen to prevent atelectasis. Important prophylactic in operations—La Flèche, *Brit. med. J.*, ii/1930, 526.

Carbon dioxide 5% (some employ even 25%) with oxygen as a control of respiration in anæsthesia; also in asphyxia of the new-born, alcoholic intoxication and carbon monoxide asphyxia. The mixture is not used "straight" but is added to air or oxygen from another cylinder.—Yandell Henderson, *Brit. med. J.*, ii/1925, 1170. See also *ibid.*, 1181 *et seq.* and 1186.

**ANGINA PECTORIS** benefited by inhalation daily for 15 minutes from an open mask.—*Brit. med. J. Epit.*, ii/1931, 26.

**PNEUMONIA.** In the absence of respiratory failure, as evinced by shallow breathing, the clinical benefits of CO<sub>2</sub> administration are not sufficiently demonstrated to warrant its routine use in lobar pneumonia.—R. Hilton, *Brit. med. J.*, i/1934, 420.

**WHOOPIING COUGH.** Dyspnoea and cyanosis immediately relieved in a child of 8 weeks by spraying a little gas on the face.—J. Dunlop, *Brit. med. J.*, ii/1932, 822. Also in spasmodic asthma and chronic rhinitis.—G. Willett, *ibid.*, 1996.

**"Carbonic Snow,"** i.e., carbon dioxide in the semi-solid condition, formed as the gas evaporates from a storage cylinder, is much employed therapeutically. The cylinders contain CO<sub>2</sub> at a pressure of about 950 lbs. to the square inch (65 atmospheres), yield the snow on opening with a temperature of -79°C. (-110°F.), which by collecting in a suitable receptacle can be formed into a stick or crayon like an ordinary candle, or may be compressed into a mould and cut any shape with a knife. The cylinders should be mounted on a stand with the stopcock on a lower level than the opposite end so that the liquid gas covers the inner orifice of the valve.

**Crayons, Method of making.** The snow evaporates slowly—a crayon 5 by 1 inch will last about 1 to 2 hours. As many as thirty applications with this size can be made. The temperature of the crayon is constant. A towel is folded into three and wrapped round an ordinary ruler—the ruler is then removed and the tube thus produced is bound on to the valve of the CO<sub>2</sub> cylinder, the gas is turned on and the towel tube fills with the snow. The frozen gas may then be pressed into a piece of vulcanite or celluloid tubing about 1 inch in diameter with a ruler. A cardboard postal tube or roll of blotting paper (several thicknesses) will also serve. Cover end of crayon with lint for handling. Can be pointed with a pen-knife or shaped by rubbing against the side of a vessel containing hot water.

An old glove finger has been suggested for collecting the CO<sub>2</sub> by tying on to the vent of the cylinder. When completely filled and rigid, remove and with a sharp knife cut the end of the finger off at about 1½ inches from the point, thus exposing a corresponding length of the crayon, which can be used to the part, the rest of the glove finger serving as a holder.

**Uses.** For removal of nævi, moles and blemishes, lupus erythematosus, lupus vulgaris, rodent ulcer, and warts (for last mentioned long application necessary). Also employed for trachoma and chronic localised eczema. A single application usually suffices. The thawing out is usually more painful than the freezing.

**ALOPECIA AREATA** of 3 to 7 years' duration has been well treated. Hair grows after three or four applications within 3 weeks.

**CORNEAL ULCERS.** The surface of the ulcer is carefully touched. Cocaine is not necessary. If patient complains of discomfort the eye can be bathed with cold boracic lotion. The surface of the ulcer becomes white and raised; within 24 or 36 hours this "slough" separates, leaving a clean healing ulcer. Infiltrations disappear from the surrounding healthy cornea and hypopyon vanishes. After treatment, pads and bandages are used instead of fomentations, and atropine sulphate 1% is instilled once daily. The method is not advised for marginal or ring ulcers.

**KERATOSIS** accompanying X-ray dermatitis. Brief applications answer well. The treated area becomes firmer and in 2 or 3 minutes swollen. A wheal forms with acute hyperæmia within half an hour and a vesicle usually within an hour; applying 30 seconds or longer, this will almost certainly be followed by scarring. An intense superficial destruction is obtained by a second application immediately after the tissues have thawed out.

Boric ointment is used for after-treatment. If blister forms, the fluid is removed within a few days; the crust forming should be allowed to fall off. The scar ultimately is pale, soft and pliable.

**NÆVI.** In the case of an ordinary capillary nævus the crayon is roughly shaped to that of the nævus—or slightly larger; it is applied and firmly pressed down for, on an average, 40 seconds. If there is bone immediately beneath, a shorter time will do. For a cavernous nævus the end of the crayon is made the same size or slightly smaller than the area of the growth. A long application with deep pressure should effectually freeze the whole mass.

The treatment of strawberry nævi with  $\text{CO}_2$  snow.—H. C. Semon, *Lancet*, i/1934, 1167.

Carbon dioxide snow offers a satisfactory and inexpensive means for the treatment of hemangiomas in children. The results in small thin lesions are excellent, but as the size and depth increase they become progressively worse, so that in large deep lesions the results by this method of treatment are poor.—N. M. Wrong, *Canad. med. Ass. J.*, ii/1939, 571.

**PSORIASIS.** Patches removed by 30 seconds' application.

**RODENT ULCER.** Early rodent ulcers up to the size of a shilling treated as follows:—

Ring the ulcer with Novocain 2% and firmly scrape with a sharp spoon; the tumour comes away and a clean raw area is left. Apply a pencil of  $\text{CO}_2$  snow for 60 seconds and then a dry dressing. There is œdema for a day or two but practically no pain, and the ulcer heals rapidly under boric ointment. The resulting scars are very smooth and fine. Recurrences infrequent and successfully treated by a repetition.—J. F. Smith, *Brit. med. J.*, ii/1928, 443.

Although it has occasionally cured a case, its use on the whole is most unsatisfactory. It is painful and produces scarring, and the proportion of failures is too great to make it permissible to use it.—N. S. Finzi, *Brit. med. J.*, ii/1933, 137.

**TRACHOMA.** The method may be applied energetically in trachoma without risk. The lid is everted and separated from the globe by a non-conducting spatula—the pencil is lightly pressed down on to the part of the conjunctiva to be treated for 15 to 30 seconds.

**Carbonei Disulphidum** (B.P.C., *P. Helv. V*). *Syn.* CARBON BISULPHIDE, CARBO SULFURATUS (*Fr. Cx.*).  $\text{CS}_2 = 76.12$ .

A clear liquid with characteristic odour, sp. gr. 1.268 to 1.272, b.p.  $46^\circ$ , flash point  $20^\circ$ .

Almost *insoluble* in water, but readily in alcohol, ether and chloroform and the fixed and volatile oils. Dissolves phosphorus, sulphur and rubber with avidity.

The vapour mixed with air in the proportions of from 1 to 50% is explosive when brought in contact with a flame or a steam-pipe. Exposure for  $\frac{1}{2}$  hour to a concentration of 0.35% may cause severe illness.

**Antidotes.** Keep patient in bed and warm. Oxygen inhalations if necessary. On recovery from the comatose condition, the patient may become maniacal and must be controlled.

**CHRONIC POISONING IN INDUSTRY.** Absorption takes place both through the lungs and the skin, and the poison is cumulative. A concentration of 1 in 3000 in air will produce a headache after a few hours' exposure.

Inhalation of small quantities of the vapour over some weeks or months produces chronic effects, the first of which are nausea, headache and giddiness, fetid breath, pallor, and a pale and flabby tongue. Later symptoms include mental disturbances with impaired memory and depression, muscular weakness,

tremor, loss of sensation, and optic neuritis. Acute poisoning produces severe mental disturbance, possibly acute mania. In chronic poisoning some of the symptoms may continue after removal of the patient from toxic exposure.—(Memorandum on precautions against dangers of poisoning, fire and explosion associated with the use of carbon bisulphide in artificial silk, india-rubber, and other works.) H.M.S.O., Form 836, 1936.

The most usual form of insanity due to carbon disulphide poisoning is the manic-depressive type, which lasts for some months or a year or two, then usually clears up, but in some cases passes into lasting dementia. Dimness of vision is a common symptom, the lesion produced being a retrobulbar neuritis with atrophy of the optic nerves; this is sometimes transient and sometimes results in permanent loss of visual acuity. A form of Parkinson's disease, with a tremor like that of paralysis agitans, is reported from Italy. A polyneuritis, affecting the nerves of the lower extremities, has also been described and sexual impotence is a very common symptom in men.—A. Hamilton, *New Engl. J. Med.*, 1936, 215, 426.

Report of six cases of poisoning in the rayon industry. The concentration of carbon disulphide in the atmosphere should be kept around 10 parts per million (0.03 mg. per litre).—S. T. Gordy and M. Trumper, *J. Amer. med. Ass.*, i/1938, 1543.

**Uses.** Has been used as an external application in enlarged lymphatic glands, employing a wide-mouthed bottle containing a fluid drachm of carbon disulphide imbibed by a piece of sponge, the skin over the gland having been previously moistened with water. It has also been used in a similar manner in facial neuralgia and other local pains.

**DIARRHŒA.** Has been used as a remedy for diarrhœa in doses of 30 ml. of a 3.5% solution 4 to 5 times a day.—J. W. Tomb, *Brit. med. J.*, i/1934, 1097.

## CHLORINATED HYDROCARBON COMPOUNDS.

(for Methyl and Ethyl Chlorides, see under *ÆTHYLIS CHLORIDUM*)

**Carbonei Tetrachloridum** (*B.P.*, *U.S.P. XI*, *Fr. Cx.*, *P. Jap. V*, *P. Ned. V*, *F.E. VIII*). *Syn. and Prop. Name.* TETRACHLOR-METHANE, TETRAFORM (*British Drug Houses, London*).  $\text{CCl}_4$  = 153.83.

**Dose.**— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.). 6 ml. doses have been taken by an adult. 10 to 20 minims is safe for children of 3 to 4 years. Children of 1 year can have 10 minims; a child of 10 should receive 30 minims; a youth of 16, 40 minims ( $2\frac{1}{2}$  ml.), and so on even when seriously ill from various causes. *U.S.P. XI* average dose (caution) 40 minims. Milk is the best vehicle even if given in capsule. Must not be given in spirit or turpentine.

A heavy, volatile, and mobile chloroform-like liquid, has a pleasant, pungent, quince-like odour if pure; not inflammable.

**Insoluble** in water; soluble in organic solvents and fixed and volatile oils.

**Antidotes.** (Swallowed.) Empty stomach by emetic or stomach tube. Keep patient lying down and warm. Give purgative dose of magnesium sulphate. Dextrose and fluids freely, but not oils or fats. (Inhaled.) Keep patient warm. Artificial respiration. Respiratory stimulants.

Deaths after carbon tetrachloride have occurred in Jamaica, and thymol is now the drug of choice against hookworms.—B. M. Wilson, *Brit. med. J.*, ii/1928, 207. Carbon tetrachloride a proved potent liver poison and should not be given to a purged and fasting patient unless sufficient glucose is given at the same time.—H. M. Hanschell, *ibid.*

**Poisoning due to production of hypoglycæmia.** Relieved by intravenous calcium therapy.—A. S. Minot, *ibid.*, 1931, 312.

Its use in hairdressing (for making the hair look clean and glossy) is reprehensible on account of the risks of serious poisoning. Two cases recorded.—*Brit. med. J. Epit.*, 1/1933, 5.

**Uses.** It has been extensively used in ankylostomiasis (hookworm infection). The dose should be taken in the morning on an empty stomach. A mild laxative should be given the day before, and a purgative dose of magnesium sulphate three hours after the anthelmintic. To ensure complete removal of the worms a test dose of 3 ml. of chenopodium oil may be given a week later. Alcohol should be avoided during treatment, and the drug is contraindicated in the presence of disease of the heart, liver or kidneys and in alcoholic subjects. The combined use of carbon tetrachloride 2 ml., and oil of chenopodium 1 ml., has found much favour and is stated to be more effective and less toxic.

More than 100,000 consecutive treatments of hookworm disease without a death, and with few untoward symptoms.—S. M. Lambert, *J. Amer. med. Ass.*, 1/1933, 248.

Many hundreds of cases of hookworm treated as a routine measure every six months without complaints even of discomfort. The method of administration recommended is to give 3 ml. of carbon tetrachloride (Tetraform) in 15 ml. of castor oil (or liquid paraffin). No purgative is needed after its use.—A. S. Tuxford, *Lancet*, 1/1935, 1302.

A resurvey of hookworm disease in Fiji in 1935, 10 years after mass treatment with carbon tetrachloride, indicated that infection was only half of what it had been before the treatment campaign, and that infection was less severe in form. After 10 years there were still few clinical manifestations of hookworm disease in areas where formerly there had been almost universal anæmia.—S. M. Lambert, *J. trop. Med. (Hyg.)*, 1936, 21.

**TAPEWORM.** Carbon tetrachloride is the most effective remedy for the treatment of tapeworm infestations in man, the usual dose being 4 ml. It is superior to male fern, not only in efficiency, but in being less inconvenient, less time-consuming, and less expensive. Alcohol and fat should be avoided for at least a day before and after treatment, and there should be prompt purgation within a few hours.—J. H. Sandground, *New Engl. J. Med.*, 1/1938, 298.

**Diphenan.** *Syn. and Prop. Names.* *p*-BENZYLPHENYL CARBAMATE, BUTOLAN (Bayer Products, London), OXYLAN (Burroughs Wellcome, London).  $C_6H_5 \cdot CH_2 \cdot C_6H_4 \cdot O \cdot CO \cdot NH_2$ , = 227.2.

Carbamic acid ester of *p*-hydroxydiphenylmethane, in white, odourless, tasteless crystals, slightly soluble in water. For oxyuriasis (thread-worm). *Dose.*—1 or 2 tablets ( $7\frac{1}{2}$  grains each) three times daily for one week.

The drug is singularly free from toxic effects, but may cause diarrhoea. It is wise to wash out the colon with quassia infusion daily, to administer dilute hydrochloric acid by mouth, and to smear the perianal region with a weak mercury ointment.—Hale-White.

**Dichlorethyleneum (B.P.C.).** *Syn.* ACETYLENE DICHLORIDE.  $C_2H_2Cl_2$  = 96.93.

A heavy mobile liquid, with slightly acid ethereal odour, consisting of a mixture of two stereoisomers boiling at 48° and 60°, and having sp. gr. of about 1.30. It is not readily inflammable and is suggested to replace ether for laboratory use. It is the best known solvent for rubber.

Is employed as a solvent of iodine for sterilising the skin. 2.5% *w/v* is used, i.e., practically a saturated solution. This solution is said to cause the operating surgeon or assistants no lachrymation or catarrh of the nasal mucous membrane which the methylated spirit tincture produces.

**Ethyleni Dichloridum (B.P.C.).** *Syn.* DICHLORETHANE.  $C_2H_4Cl_2$  = 98.95. A mobile liquid with ethereal odour and sweet taste. B.p. 84°. Used as a solvent of iodine (1 in 40) for skin disinfection.

**Trichlorethylene.** *Prop. Name.* CHLORYLEN (*Schering, London*).  
CHCl : CCl<sub>2</sub> = 131·4. Colourless liquid b.p. 88°, sp. gr. 1·47.

**Uses.** For trigeminal neuralgia 10 to 20 minims may be inhaled from cotton wool. Not more than 60 minims in twenty-four hours. It has also been found of value in the prevention and treatment of attacks of angina pectoris, but it should always be taken with the patient lying down and should not be used as a substitute for amyl nitrite in the acute attack. Externally, it is a useful cleansing agent for dirty and greasy wounds. To remove the smell wash well with a strong solution of potassium permanganate and with water. An ointment, 1 in 4, in soft paraffin, destroys body lice, and soap solutions containing 2% may be used for cleaning the body.

Used in commerce for the solution of tarry, bituminous products, rubber, sulphur, phosphorus, and for dry cleaning.

At first several fatalities were ascribed to exposure to its vapour, but these were in fact due to impurities or disintegration products. Since 1930 the process of manufacture has been so perfected, and the discovery of stabilisers so advanced, that the trichlorethylene of commerce is now a pure and stable substance, and since that date no trace of any fatality ascribed to it can be traced.

A powerful "degreaser," and as a wound cleanser greatly superior to surgical spirit, methylated spirit, etc. It is also a good solvent for tar and is particularly useful in the treatment of tar burns. A boy of 9 playing with a tar-spraying machine received very extensive burns; following cleansing with trichlorethylene and coagulation with Tannafavine he made an uninterrupted recovery.—H. B. Trumper, *Brit. med. J.*, ii/1934, 1219.

Applied as a spray it is a useful cleansing agent for all dirty and greasy wounds, including tar burns. As it has no effective antiseptic power *per se*, the wound should be dressed with a recognised antiseptic after the preliminary cleansing.—H. B. Trumper, A. T. Jones and H. Taylor, *Lancet*, ii/1936, 1390.

**ANGINA PECTORIS.** Inhalation of 1 ml. morning and evening relieved the distress and apprehension in most cases.—J. C. Krantz, *J. Amer. med. Ass.*, i/1936, 485.

Results rather disappointing; of 40 cases treated only one obtained complete relief, and in 13 cases no improvement was noted. Should be given a trial when other methods have failed. The inhalations are safe and well tolerated.—F. A. Willius and F. J. Dry, *Amer. Heart J.*, 1937, 659.

**TIC DOULOUREUX.** From 10 to 50% of patients are benefited by inhalation of doses of 25 to 35 drops four times daily, continued for two or three weeks. If no relief results at the end of that time it is useless to continue the treatment. There is risk of damage to the liver if the drug is used over many months.—P. G. Flothow, *per Prescriber*, 1939, 137.

**Tetrachlorethylenum (B.P.C.).** *Syn.* PERCHLOR-ETHYLENE.  
C<sub>2</sub>Cl<sub>4</sub> = 165·8.

**Dose.**—15 minims (1 ml.) in capsules. For ankylostomiasis doses totalling 3, 4 and 5 ml. are given at hourly intervals on each of three consecutive days; on the third day, 3 hours after the last dose, give saline purge.

Colourless heavy mobile liquid with odour similar to that of carbon tetrachloride. B.p. 117° to 122°; sp. gr. about 1·62.

**Insoluble** in water; miscible with alcohol 90%, ether and oils. Used for the expulsion of hookworm in man and animals and of roundworms in animals. It is stated to be as effective as carbon

tetrachloride against hookworm without its toxicity. Its use should be followed by a saline purgative, and patients should remain in bed and drink plenty of milk; alcohol should be avoided.

**ANKYLOSTOMIASIS.** An extremely valuable substance for the treatment of uncomplicated hookworm disease. Thought to be as effective against hookworm as carbon tetrachloride, but should not be classed with the latter as a toxic anthelmintic. Ineffective against ascaris.—P. D. Lamson and co-workers, *J. Amer. med. Ass.*, ii/1932, 293.

Much less toxic in cats than carbon tetrachloride and harmless in therapeutic doses. A mixture of 2 ounces of saturated magnesium sulphate with 4 ml. of tetrachlorethylene and 1 ml. of oil of chenopodium, shaken to form a fine emulsion and given immediately, gave 62% of cures with one treatment in 50 cases.—P. A. Mapleston, A. K. Mukerji and R. N. Chopra, *Indian med. Gaz.*, 1933, 554 and 617.

More than 46,000 treatments of hookworm disease without a death, and with few untoward symptoms. The most satisfactory anthelmintic so far developed for hookworm disease.—S. M. Lambert, *J. Amer. med. Ass.*, i/1933, 248.

Tetrachlorethylene is a safe and reliable anthelmintic for general use when properly administered. Potency increased by addition of oil of chenopodium.—D. Manson, *Indian med. Gaz.*, 1934, 500.

Doses of 4 to 5 ml. may be safely given to adult patients and two such treatments at intervals of 10 days may be expected to cure even severe cases of ankylostomiasis. Children may be given tetrachlorethylene in doses of 4 to 5 times the age in minims. No appreciable toxic action has been found even after 8 ml. doses on the cardiovascular, respiratory, hepatic, and renal organs.—P. B. Fernando, *Indian J. med. Res.*, 1939, 26, 759.

**OXYURIASIS.** Tetrachlorethylene is one of the best drugs for a single-dose treatment for pinworms. It is especially effective for light pinworm infestations, but will probably fail to effect cures in the majority of persons heavily infested. The tetrachlorethylene is administered at a dose rate of 0.1 ml. for each year of apparent (not chronological) age, the drug being given in a suitable dose of a solution of magnesium citrate (which gives rise to fewer reactions than magnesium sulphate).—W. H. Wright, *J. Amer. med. Ass.*, ii/1937, 570.

**Tetrachlorethane.** *Syn.* ACETYLENE TETRACHLORIDE.

$C_2H_2Cl_4 = 167.8$ .

A liquid with penetrating odour, b.p. about  $146^\circ$ ; sp. gr. about 1.6. It dissolves oils, fats, waxes, and resins, and sulphur (1% at ordinary temperature), phosphorus and chlorine.

Used as a solvent for varnishes, especially cellulose acetate, and as a paint-remover and degreaser. Extensively employed as an insecticide, especially for white fly on tomato plants and for weevils, 10 fl. oz. being allowed to volatilise for 1000 cu. ft.

**Pentachlorethane,**  $C_2HCl_5 = 202.3$ , is similar. B.p.  $159^\circ$ .

**Hexachlorethane.**  $C_2Cl_6 = 236.7$ .

A solid subliming at  $185^\circ$  without melting; almost insoluble in water, more soluble in alcohol and ether, or a mixture of the two. It has a smell similar to camphor, for which it is used as a substitute in the celluloid industry. Also employed to render substances non-inflammable in explosives industry, and is incorporated in anti-fouling paints.

## CARYOPHYLLUM

(with CARDAMOMUM, etc.)

B.P., U.S.P. XI, Fr. Cx., P. Dan.

**Dose.**—2 to 5 grains (0.12 to 0.3 g.).

The dried flower-buds of *Eugenia aromatica* (Myrtaceæ) (*E. caryophyllata*).

In senile flatulence good effects are produced by powdered cloves, better even than a fluid preparation. Spirit of cloves is absorbed in the stomach but the woody fibre passes on to the seat of the complaint.

**Aqua Caryophylli Destillata (B.P.C.).** Dose.— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.), 1 in 40.

**Aqua Caryophylli Concentrata (B.P.C.).** Dose.—5 to 15 minims (0.3 to 1 ml.). Contains 2% v/v of oil of clove and is approximately 40 times the strength of the distilled water.

**Infusum Caryophylli Concentratum (B.P.).** Dose.— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.). 1 in 5.

**Infusum Caryophylli Recens (B.P.).** Dose.— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.), 1 in 40.

**Tinctura Caryophylli.** 1 in 8 of alcohol 90%. Digest 10 days. Dose.—20 to 40 minims or more: aromatic, carminative and stimulant.

**Oleum Caryophylli (B.P., U.S.P. XI, Fr. Cx., P. Jap. V, P. Helv. V).**

Dose.—1 to 3 minims (0.06 to 0.2 ml.).

Colourless to brownish oil. Contains 85 to 90% v/v of eugenol,  $C_{10}H_{12}O_2$ . Soluble 1 in 2 of alcohol 70%.

Internally, oil of cloves is antispasmodic and carminative, and may be employed in doses of 3 to 5 minims to relieve flatulence and to reduce expectoration, especially in phthisis. Externally, it is rubefacient and slightly anæsthetic, and may be applied, mixed with olive oil, to neuralgic areas. It is a useful domestic remedy for toothache, a plug of cotton wool soaked in the oil being inserted in the cavity of the carious tooth.

**NEURALGIA.** A useful household remedy to keep in reserve for the pain of a carious tooth is oil of cloves, either alone, or better still, added to equal parts of carbolic acid and menthol. The carious cavity is mopped out with a fine probe, e.g., a pointed match stick with a little wool twisted round it, and a tiny piece of cotton wool soaked in the solution gently pressed into the cavity. This will usually arrest the pain for several hours.—Wilfred Harris, *Practitioner*, i/1940, 320.

**Eugenol (B.P.C., U.S.P. XI, P. Dan.).** Syn. EUGENIC ACID, 2-METHOXY-4-ALLYLPHENOL.  $C_9H_9(OH)(OCH_3) \cdot C_2H_5$ , 4:3:1 = 164.1.

Dose.—1 to 3 minims (0.06 to 0.2 ml.).

A colourless oily liquid, b.p.  $251^\circ$  to  $253^\circ$ ; U.S.P. XI  $250^\circ$  to  $255^\circ$ ; darkening on exposure. It is the chief constituent of oil of clove and has a strong clove odour. Is a powerful antiseptic and antiputrescent. Is employed by dentists as an abundant causing reduced sensibility of mucous membrane, but not complete anæsthesia. Useful with wool fat in eczema.

**Isoeugenol**, used in perfumery for its carnation-clove odour and for the manufacture of vanillin, is obtained by heating eugenol with potassium hydroxide.

**Cardamomum (B.P., U.S.P. XI, P. Helv. V).** Syn. CARDAMOMI SEMINA, FRUCTUS CARDAMOMI (P. Dan., P. Jap. V).

The dried ripe seeds of *Elettaria Cardamomum* var. *minuscule* (Zingiberaceæ). The seeds should not be removed from their fruits until required for use. Given in atonic dyspepsia. Contained in Pulvis Aromaticus.

**Tinctura Cardamomi Aromatica (B.P.C.).** Syn. TINCTURA CARMINATIVA. Dose.—2 to 10 minims (0.12 to 0.6 ml.).

Cardamom about 1 in 16 with strong tincture of ginger and oils of caraway, cinnamon and clove.



**Tinctura Cardamomi Composita (B.P.).**

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.). Cardamom 1.4% with caraway, cinnamon, cochineal, glycerin and alcohol 80%. Is more or less decolorised by alkaloidal salts, bismuth oxide, oxycarbonate and subnitrate; also by metals of the alkaline earths and sodium bromide: employ Liquor Bismuthi in preference.

**Tinctura Cardamomi Composita (U.S.P. XI).**

*Average dose.*—60 minims (4 ml.).

Cardamom seed 2, cinnamon 2.5, caraway 1.2, cochineal 0.5, glycerin 5, in diluted alcohol to 100.

**Oleum Cardamomi (B.P.C.).** *Dose.*— $\frac{1}{2}$  to 3 minims (0.03 to 0.2 ml.).

Obtained from the whole fruits of cardamom. Aromatic carminative.

**Carum (B.P., U.S.P. XI). Syn. CARUI FRUCTUS, CARAWAY FRUIT OF SEED.**

*Dose.*—10 to 30 grains (0.6 to 2 g.). The dried ripe fruits of *Carum Carvi* (Umbelliferae). An aromatic carminative of value in flatulent colic, especially in children.

**Aqua Cari Destillata (B.P.C.).** *Syn. AQUA CARUI DESTILLATA.* *Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.). 1 in 10.

**Aqua Cari Concentrata (B.P.C.).** *Dose.*—5 to 15 minims (0.3 to 1 ml.). Contains 2% v/v of oil of caraway and is approximately 40 times the strength of the distilled water.

**Oleum Cari (B.P., P. Helv. V). Syn. OLEUM CARUI.**

*Dose.*—1 to 3 minims (0.06 to 0.2 ml.).

Contains 53 to 63% w/w of carvone,  $C_{10}H_{14}O$ . Soluble 1 in 1 of alcohol 90% and 1 in 7 of alcohol 80%.

Carvone,  $C_{10}H_{14}O$ , the principal constituent of oil of caraway, occurs also in oils of dill and spearmint. It is a colourless or slightly yellow liquid, miscible with alcohol.

**Coriandrum (B.P., Fr. Cx., P. Dan.).**

*Dose.*—5 to 15 grains (0.3 to 1 g.).

Dried ripe fruits of *Coriandrum sativum* (Umbelliferae). Aromatic and carminative.

**Oleum Coriandri (B.P.).** *Dose.*—1 to 3 minims (0.06 to 0.2 ml.). Is added to preparations of rhubarb and senna to prevent griping. The flavour becomes less pleasant on keeping.

**Myrica (B.P.C.). Syn. BAYBERRY, WAX MYRTLE BARK.**

*Dose.*—10 to 60 grains (0.6 to 4 g.).

The dried root-bark of *Myrica cerifera* (Myricaceae). Tonic and astringent, emetic in large doses. Is an ingredient, together with various proportions of ginger, capsicum and clove, of COMPOSITION POWDER or COMPOSITION ESSENCE used as a domestic remedy for colds.

**Myricin.** *Dose.*—2 to 5 grains. The powdered extract of *Myrica cerifera*. An astringent and stimulant, and in large doses, emetic. For diarrhoea and jaundice.

**Myristica (B.P., U.S.P. XI, P. Helv. V, P. Jap. V). Syn. NUX MOSCHATA, NUTMEG, MUSCADE (Fr. Cx.).**

*Dose.*—5 to 10 grains (0.3 to 0.6 g.). The dried kernels of the seeds of *Myristica fragrans* (Myristicaceae). An aromatic carminative. From one to one and a half nutmegs, or a teaspoonful of powdered mace, have caused severe poisoning symptoms.

**Oleum Myristicæ (B.P., U.S.P. XI).** *Dose.*—1 to 3 minims (0.06 to 0.2 ml.). Distilled from nutmeg. Soluble 1 in 3 of alcohol 90%.

**Oleum Myristicæ Expressum.** *Syn. ADEPS MYRISTICÆ, BUTYRUM MYRISTICÆ (Fr. Cx.), MACE BUTTER.*

Bright orange, solid fat obtained from nutmeg or mace by hot expression. Soluble in ether, alcohol and chloroform. Is a mild stimulant and has been incorporated in plasters.

The expressed or concrete oil of nutmeg of yellowish colour contains myristicin,  $C_{15}H_{21}O_2 = 206.1$ . It is occasionally employed as a gentle local stimulant. It is stated to have narcotic properties.

**Spiritus Myristicæ (B.P.C.).** Dose.—5 to 20 minims (0.3 to 1.2 ml.). 1 in 10.

**Oleum Myristicæ Deterpenatum (B.P.C.).** Terpeneless Oil of Nutmeg. Is prepared by concentration *in vacuo* and is about 5 times as strong as oil of nutmeg.

**Macis (Fr. Cx.).** Mace is the arillode of the seed of *Myristica fragrans*. It contains 7 to 14% of a volatile oil similar to oil of nutmeg.

**Oleum Myrciæ (B.P.C.).** OIL OF BAY.

Is obtained from *Pimenta acris* and other species. Occurs as a yellow liquid becoming brown on exposure to air. **Soluble** when fresh in an equal volume of alcohol 95%, less soluble on keeping.

**Spiritus Myrciæ Compositus (B.P.C.).** *Syn.* SPIRITUS PIMENTÆ COMPOSITUS.

Contains oils of bay, orange and pimento, and dry extract of quassia in diluted alcohol. Preparations of similar composition and coloured brown are sold as bay rum.

**Pimenta (B.P.C.).** *Syn.* PIMENTO, ALLSPICE, JAMAICA PEPPER.

The dried full-grown unripe fruits of *Pimenta officinalis* (Myrtaceæ).

**Aqua Pimentæ Concentrata (B.P.C.).** Dose.—5 to 15 minims (0.3 to 1 ml.). Oil of pimento 1 in 50. This preparation diluted 1 to 40 with water is to be dispensed for Aqua Pimentæ.

**Oleum Pimentæ (B.P.C.).**

Dose.— $\frac{1}{2}$  to 3 minims (0.06 to 0.2 ml.).

**Soluble** 1 in 3 of alcohol 70%; miscible with alcohol 90%. Eugenol content not less than 60% v/v. Stomachic and antispasmodic.

## CASCARA SAGRADA

*B.P., U.S.P. XI, Fr. Cx., P. Ital. V, F.E. VIII, P. Helv. V, P. Belg. IV.*

*Syn.* SACRED BARK.

Dose.—20 to 60 grains (1.2 to 4 g.) in cachets.

The dried bark of *Rhamnus Purshiana* (Rhamnaceæ).

*B.P.* and *U.S.P. XI* require the bark to be kept at least one year, but *Fr. Cx.* does not. The tree grows extensively in British Columbia.

**Uses.** Increases peristalsis and is used chiefly in chronic constipation; it is useful for piles, since it forms a soft stool and is not irritating. For dosage see Liquid Extract.

**Elixir Cascariæ Sagradæ (B.P.).**

Dose.—30 to 60 minims (2 to 4 ml.).

1 in 1, prepared by percolating with boiling water a mixture of cascara, liquorice and light magnesium oxide, evaporating, and adding alcohol, glycerin and flavouring agents. It is practically free from bitterness but is sometimes alleged to be less active therapeutically than the liquid extract.

**Fluidextractum Cascaræ Sagradæ Aromaticum (U.S.P. XI).**

*Average dose.*—30 minims (2 ml.).

Closely resembles the elixir of the B.P. 1932, but contains 0.01% of methyl salicylate and larger proportions of saccharin, oil of anise and alcohol.

*P. Ital. V* has also an aromatic liquid extract employing magnesia, with liquorice, glycerin, saccharin and anise.

**Extractum Cascaræ Sagradæ Liquidum (B.P.).**

*Dose.*—30 to 60 minims (2 to 4 ml.).

An aqueous extract containing 25% of alcohol (90%). It may be made miscible with water by adding half its volume of sal volatile.

*P. Ital. V* is very similar. *P. Belg. IV* uses 60% alcohol. *P. Jap.* makes with alcohol 90% and water equal parts. *Fr. Cx.* makes with alcohol 50%, 1 = 1 by weight using 8% of light calcined magnesia in the extraction.

*Use in Constipation.* The initial dose depends on the individual, but it must be correctly found—15 to 20 drops *t.d.* suffices for the adult. The object is to procure one motion only each day. The dose that is sufficient must be taken in a wineglassful of water thrice daily after meals for a week or ten days, or until the action becomes somewhat too pronounced. Then reduce dose by one drop only and take with the same regularity as before. In time it will be found that 1 drop in water thrice daily after meals will be sufficient. Finally the medicine may be omitted altogether.

After laparotomy, suitable aperients are confection of senna or the following: Ext. Cascara Sagrada Liq. 1 oz., sodium sulphate 1 oz., solution of ammonia 40 m., chloroform water to 8 oz. *Dose.*—2 to 4 drachms night and morning.—C. W. Gordon Bryan, *Lancet*, ii/1930, 1141.

**Fluidextractum Cascaræ Sagradæ (U.S.P. XI).**

*Average dose.*—15 minims (1 ml.).

One ml. represents 1 g. of the bark; it is of the same strength as the liquid extract of the B.P.

**Extractum Cascaræ Sagradæ Siccum (B.P.).**

*Dose.*—2 to 8 grains (0.12 to 0.5 g.) in pill.—An aqueous extract evaporated under reduced pressure, so as to produce a spongy mass which is readily granulated. *Fr. Cx.* and *P. Ital. V* extract with 60% alcohol.

*Vacuum drying of extracts.* Examination of commercial extracts of cascara, krameria and hamamelis showed that many preparations are overheated during drying, probably due to the use of steam-jacketed vacuum pans, when as the extractive thickens the portion in contact with the pan will take the temperature of the steam irrespective of any reduction of pressure employed. The degree of overheating can usually be detected by the solubility of the product in the original solvent. Vacuum ovens or pans used for drying should be heated by means of water jackets or very low pressure steam. It is suggested that the B.P. should direct dry extract of cascara to be evaporated to dryness at a temperature not exceeding 100°, and dry extract of krameria at a temperature not exceeding 70°. In both cases a limit of 10% w/w of matter insoluble in cold water should be fixed.—H. Berry and E. M. Temple, *Quart. J. Pharm.*, 1938, 364.

**Extractum Cascaræ Sagradæ (U.S.P. XI).** *Average dose.*— $\frac{1}{4}$  grain (0.015 g.). 1 g. represents 3 g. of the bark.

**Mistura Cascaræ (Gt. Orn. H.).** (For 1 year old child.)

Liquid extract of cascara, liquid extract of liquorice, syrup of orange, chloroform water, of each 15 minims for one dose.

[P1] **Mistura Cascaræ Composita (B.P.C.).**

*Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.).

Contains 20 m. of liquid extract of cascara per ounce, with tincture of belladonna and tincture of nux vomica.

[P1] **Mistura Cascaræ Composita (L.H.).** *Syn.* MISTURA APERIENTIS (L.H.).

Liquid extract of cascara sagrada 1 dr., liquid extract of senna 30 m., liquid extract of liquorice 60 m., tincture of hyoscyamus 30 m., tincture of nux vomica 10 m., emulsion of chloroform 10 m., compound decoction of aloes to 1 oz.

**Mist. Cascar.** (*N.I.F.*). Liquid extract of cascara sagrada 20 m., ammonium carbonate 2 gr., liquid extract of liquorice 20 m., chloroform water to  $\frac{1}{2}$  oz.

[P1] **Mist. Cascar. c. Nuc. Vom.** (*N.I.F.*).

Liquid extract of cascara sagrada 20 m., ammonium carbonate 2 gr., tincture of nux vomica 5 m., tincture of belladonna 3 m., liquid extract of liquorice 20 m., chloroform water to  $\frac{1}{2}$  oz.

**Mistura Hepatica.** *Dose.*—1 to 2 drachms in water. Liquid extract of cascara 20, tincture of jalap 20, tincture of podophyllum 10, compound tincture of gentian 10, chloroform water 50, sal volatile 10.

[P1-S1] **Pilulæ Cascaræ Compositæ** (*B.P.C.*). *Dose.*—1 to 3 pills; contain  $\frac{1}{2}$  gr. of dry extract of cascara with dry extracts of belladonna and nux vomica.

An agreeable and efficient aperient, with gentle action continuing beyond the first day; good for liver inaction.

**Syrupus Cascaræ Aromaticus** (*B.P.C.*).

*Dose.*— $\frac{1}{2}$  to 2 drachms (2 to 8 ml.) as laxative.

Contains 40% v/v of liquid extract of cascara flavoured with orange and cinnamon.

**Tabellæ Cascaræ Sagradæ** (*B.P.C.*) contain 2 gr. (0.12 g.) of the dry extract.

**Tinctura Cascaræ Sagradæ** (*Fr. Cx.*).

*Laxative Dose.*—10 to 60 minims (0.6 to 4 ml.).

Percolate 1 to 5 with alcohol 60%.

[P1] **Tinctura Laxativa.**

*Dose.*—20 to 60 minims (1.2 to 4 ml.).

Liquid extract of cascara sagrada 2, aromatic spirit of ammonia 2, spirit of chloroform 2, tincture of belladonna 1, tincture of nux vomica 1. This is an agreeable and elegant form of administering cascara, being miscible with water.

**Trochisci Cascaræ Sagradæ et Olei Menthe Piperitæ.**

These are made with fruit basis, and contain  $2\frac{1}{2}$  gr. of extract flavoured with peppermint; they are useful correctives. *Dose.*—1 or 2.

**Vinum Cascaræ.**

*Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.).

Liquid extract of cascara 1, sugar 1, aromatic elixir 1, sherry-type wine to 20. Mix and decant from any sediment which may form on standing.

**Cascara Evacuant** (*Parke, Davis, London*). Palatable cascara preparation. *Dose.*—10 to 30 minims.

**Cascaromat** (*Evans, Sons, Lescher & Webb, Liverpool*). An aromatic preparation of cascara sagrada free from bitterness.

[P1-S1] **Hepatagen** (*Hewlett, London*). Contains extract of cascara, extract of rhubarb, jalapin, podophyllin, cocaine hydrochloride, aromatics, etc.

*Dose.*—10 to 60 minims. In biliousness, hepatitis and chronic gastritis.

**Kasak** (*Squire & Sons, London*). *Dose* for children, 1 or 2 drachms; adults,  $\frac{1}{2}$  ounce. A laxative free from bitterness.

**Kasena** (*Squire & Sons, London*). Similar to Kasak but contains senna.

**Kasena Capsules** are also made.

**Molevac** (*Parke, Davis, London*). Liquid paraffin, malt extract and Cascara Evacuant (12 m. per oz.). *Dose.*—From one teaspoonful. Chronic constipation.

**Peristaltin** (*Ciba, Horsham*). Water-soluble glycosides of cascara sagrada. Supplied in tablets containing  $1\frac{1}{2}$  gr. and ampoules of 1.5 ml. (=  $2\frac{1}{2}$  gr.). *Dose.*—1 to 3 tablets daily or 1 or 2 ampoules daily hypodermically or intravenously. In chronic constipation and post-operative intestinal paresis.

**Dihydroxyanthraquinone.** *Syn. and Prop. Name.* DIOXYANTHRACHINONUM (*P.G. VI*); ISTIN (*Bayer Products, London*) is dihydroxyanthraquinone in 0.15 g. tablets.  $\text{HO}-\text{C}_6\text{H}_3\text{CO}-\text{CO}-\text{C}_6\text{H}_3-\text{OH} = 242.1$ .

*Dose.*—2 to 6 grains (0.12 to 0.4 g.).

Orange crystalline powder, slightly soluble in water. M.p.  $190^\circ$  to  $192^\circ$ . A synthetic purgative.

**Immidiol** (*Napp, London*). A mixture of anthraquinone glucosides in an alcoholic solution of salicylic acid. Advocated for use as a gargle diluted about 1 in 80 in the treatment of various anginas of the mouth and throat. The preparation may also be applied undiluted as a spray or paint.

**Isacen** (*Roche Products, Welwyn Garden City*) is DIACETYL-DIHYDROXY-PHENYL-ISATINE, a synthetic purgative, which in small doses stimulates peristalsis by action upon the mucous lining of the colon and large intestine. It passes through the stomach unchanged and has no action upon the kidneys.

*Dose*.—1 to 4 granules, each  $\frac{1}{2}$  grain (0.005 g.)

**Frangula** (*B.P.C., P. Helv. V, P. Dan.*). *Syn.* ALDER BUCKTHORN BARK, BOURDAINE (*Fr. Cx.*).

The bark from the stem and branches of *Rhamnus Frangula* (*Rhamnaceæ*). Indigenous to Europe and America. Should be one year old. Cathartic especially for hemorrhoids and chronic constipation; resembles cascara in constituents and action. Liquid Extract *B.P.* '85 (1 = 1). *Dose*.—1 to 4 drachms. *Fr. Cx.* liquid extract is 1 in 1 with alcohol 30%.

*Rhamnus* (*B.P.C.*). *Syn.* BUCKTHORN, NERPRUN (*Fr. Cx.*).

The fresh ripe fruit of *R. cathartica* (*Rhamnaceæ*).

**Syrupus Rhamni** (*B.P.C.*). *Dose*.— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.). A solution of sucrose in the juice expressed from buckthorn, with oil of pimento. A laxative, used chiefly in veterinary practice.

**Normacol** (*Norgine Pharmaceutical Products, London*).

*Dose*.—1 to 2 drachms in a glass of water once or twice daily.

A preparation of dried plant mucilage of the bassorin type containing a little buckthorn extract. For treatment of habitual constipation.

Bassorin is the name given to the insoluble portion of many gums karaya, tragacanth, etc. It swells up with water, but is not soluble.

**Juglandin**. An extractive prepared from the inner bark of the root of *Juglans cinerea*, the North-American butter nut; is an hepatic stimulant and cathartic. *Dose*.—2 to 5 grains in pill. **Spiritus Nucis Juglandis**, distilled from *Juglans regia*, the common European walnut, is an antispasmodic and has been used for checking sickness of pregnancy. *Dose*.—1 to 4 drachms. **Folia Juglandis** are in *P. Austr.*; also in *P. Belg.* (and Fluid Extract) and *P. Helv. V.*

## CASEINUM

Casein is the principle albuminoid constituent of milk, and is present in solution in the aqueous portion of the milk as an alkali-albuminate, probably as a calcium compound (the alkali in milk is about 0.5%). Some hold that casein exists as caseinogen, and that this is converted into casein by ferment. It is precipitated by dilute acids and by the enzyme, rennet. Casein is present in milk to the extent of 3 to 5% (average 3.2%). Once thrown out of solution it is not readily dissolved again, except with added alkali or hydrochloric acid.

**Uses.** Insoluble casein is largely used in industry; treated with formaldehyde and subjected to heavy pressure, it gives a very hard material similar to ebonite, which has many industrial uses.

### Caseinum Solubile (*B.P.C.*).

Soluble casein is a compound of casein with a small proportion of alkali, prepared by mixing moist precipitated casein with powdered sodium carbonate and drying at a low temperature. It is a white to yellowish-white, odourless, non-hygroscopic powder with a characteristic taste.

Almost entirely *soluble* in water.

*Incompatible* with acids.

**Uses.** Soluble casein is the chief constituent of various nutritive preparations and proprietary foods; it has the advantage of being more readily miscible with water and more easily digested. It is also employed as a constituent in non-greasy skin creams.

A mixture of amino-acids has been given intravenously to human beings for parenteral protein alimentation. The mixture was obtained by the acid hydrolysis of casein, to which was added 2% tryptophane and cystine (or methionine). No evidence of toxicity either clinically or histologically was observed when the injection was given slowly, even though as much as 2 g. per Kg. was injected. Experimental and clinical observations have indicated that the injected amino-acids are rapidly utilised; this was shown by nitrogen balance studies, by regeneration of serum protein and by reduction of nutritional oedema.—R. Elman and D. O. Weiner, *J. Amer. med. Ass.*, i/1939, 796.

**SYNTHETIC MILK.** For use when milk is forbidden, as in a strictly salt-free diet, has been prepared from water, lactose, cream, "ashless" casein ("a special acid-washed first grade acid casein"), and a salt mixture containing calcium, magnesium, potassium, iron and phosphorus. A salt-free bread containing 19.7% of protein may also be prepared, using "ashless" casein.—E. M. Widdowson and R. A. McCance, *Lancet*, i/1935, 1437.

**Pigmentum Casein.** *Syn.* UNGUENTUM CASEINÆ. Casein 14, potassium carbonate  $\frac{1}{2}$ , glycerin 7, soft paraffin 21, zinc oxide  $\frac{1}{2}$ , phenol  $\frac{1}{2}$ , water to 100. If good casein be used this is almost too thick—add a little more water. A basis for skin medicaments. Thymol *q.s.* may be added to preserve it.

**Fissan Brand Products** (*Genatosan, Loughborough*). A series of preparations including dusting powders, ointments, etc., whose base is an "albumin colloid isolated from milk," which is rendered especially effective by means of a light powder, "fluoro-silica colloid."

### Notes on Artificial Feeding with Cows' Milk and Casein Products.

**Human milk** has the average composition:—Fat 3.4%, lactose 6.4%, albuminoids 1.7% (casein and lactalbumen), mineral matter 0.2%. (The difference between human milk and cows' milk in the relationship between the albuminoids and the mineral matter is dealt with in *Vol. II*.)

If artificial feeding has to be resorted to, Tuberculin Tested cows' milk (*see Vol. II*) should first be tried, as a general rule diluted with an equal quantity of water. Milk sugar, a drachm to the pint, is also a useful addition. The product contains approximately the same proportion of protein as human milk but is low in fat and sugar.

**Artificial human milk** may be made from diluted milk by addition of cream, or other fat, and lactose. To 4 oz. of diluted milk add 1 teaspoonful of lactose and 1 teaspoonful of cream (Hutchison & Mottram, *Food and Principles of Dietetics*). Instead of adding cream, "upper milk" may be used instead of whole milk. This consists of the upper portion of milk that has stood in a cool place until a cream layer has formed. By diluting with water, or with water and whole milk, mixtures are obtained containing a high percentage of fat with a normal percentage of protein. Upper milks are much superior to cream mixtures for feeding—the fat percentages are more uniform and the dilutions do not so readily separate as those employing cream.

Sodium citrate, 1 gr. per oz., may be added to prevent clotting in the stomach.

Alternatively, the extra fat may be incorporated in the form of *Emulsio Olei Arachis, B.P.C.*

Humanised milk in small quantities may be conveniently prepared by setting aside fresh cows' milk for four hours in a cool place, and separating the upper third. This is shaken, brought just to the boil and allowed to cool. After cooling, an equal volume of boiled water is added, and, for each pint, two tablespoonfuls of lactose and one ounce of lime water.—J. H. Burn, *Pharm. J.*, ii/1933, 737.

The following formula has also been employed:—Milk (of average quality) 10 oz., cream (33%) 1 oz. (or cream 48%,  $\frac{1}{2}$  oz.), sugar (lactose at first, but later lactose, maltose and cane sugar mixed) 1 oz., broth 4 oz., water to 1 pint. The addition of broth has been found good.

(For particulars of the composition of cows' and other milks, also of condensed milk, graded milks, and of the effects of pasteurisation, see Vol. II.)

### PROPRIETARY FOODS

**Allenburys Diet** (*Allen & Hanburys, London*). It is made from full-cream milk and whole wheat, with added vitamin D, and is prepared for use by the addition of boiling water or milk.

**Allenburys Foods** (*Allen & Hanburys, London*). No. 1 (for infants up to 3 months old) consists of dried milk from which excess of caseinogen has been removed and vegetable protein, lactose, and milk fat added, together with dextrin-maltose and vitamin D. No. 2 (for infants from 3 to 6 months old) is similar, but contains malted flour, free from starch. No. 3 (for infants more than 6 months old) consists of partially baked wheat flour with malt. A half-cream food and a food with additional iron are also available.

**Almata** (*Keen, Robinson, Norwich*). It is made from egg-yolk, butter-fat, dextrin-maltose, and decitrated fresh fruit juice and contains the needed mineral constituents. It is also of value as a galactagogue and an invalid food.

**Ambrosia** (*Ambrosia, London*). A dried milk powder. Also available humanised.

**Benger's Food** (*Benger's Food, Manchester*). A wheaten flour preparation containing trypsin and amylase. It is used with fresh milk or milk and water. It gives nourishment with complete or partial rest to the digestive system. The point of the preparation is that if the digestive system, however weak, can do any work at all, it should be given it to do to the extent of its power. The fat may be increased by adding cream or upper-milk.

**Brestol** (*Cow & Gate, Guildford*). "Humanised cream" with cod-liver oil and concentrated orange juice. As substitute for dairy cream and cod-liver oil emulsions in cases of fat intolerance and in backward and underweight babies, also in marasmus and tuberculosis.

**Casce** (*Mead, Johnson & Co., Evansville, U.S.A.; Brooks & Warburton, London*). Calcium caseinate, to correct diarrhoea and other nutritional disturbances of infants.

**Casumen** (*Prideaux, London*). A soluble form of casein (Flocculent Casein) containing a very high percentage of protein (90%). For use in all cases of poor nutrition. It contains practically no fat or sugar. It may be mixed with cocoa, chocolate, bread (10%) for diabetics, etc.

**Colact** (*Glaxo Laboratories, London*). Beverage of milk solids, cocoa and sugar with a concentrate of vitamins A and D. Each oz. contains 350 i.u. of vitamin A and 65 i.u. of vitamin D.

**Cow & Gate Milk** (*Cow & Gate, Guildford*). Dried milk without added sugar. Available as full-cream and half-cream.

**Energen Bread** (*Energen Foods, London*). Contains 40% of protein and only 46% of starch. Its caloric value is 108 cal. per oz. (ordinary bread 75 cal. = 1 oz.). Energen Bread and Breakfast Food (Bismel) are rich in protein and much reduced in starch, and are of value in cases requiring strict dietary.

**Farex** (*Glaxo Laboratories, London*). A preparation of wheat flour, wheat germ, oatmeal, cornmeal, edible bone meal, yeast and a concentrate of vitamins

and minerals (including calcium, phosphorus, iron, copper and vitamins A, B<sub>1</sub>, B<sub>2</sub> and D). It does not require cooking. An invalid diet and in the treatment of gastro-intestinal disorders.

**Ferrolac** (*Glaxo Laboratories, London*). Full-cream and fat-modified forms of dried milk containing 5 gr. of iron, and ammonium citrate (1 gr. of Fe) per reconstituted pint, with 200 i.u. of vitamin D (fat modified) or 165 i.u. (full-cream).

**Frailac** (*Cow & Gate, Guildford*). A reconstituted milk specially devised for frail and premature babies.

**Glaxo, Full-Cream** (*Glaxo Laboratories, London*). Resembles Sunshine Glaxo, but retains full fat and protein content of cows' milk, and contains, when reconstituted, 165 i.u. of vitamin D per pint and 5 p.p.m. of iron. For infants after first 3 or 4 months.

**Sunshine Glaxo** is adjusted to a "humanised" formula and contains when reconstituted, 200 i.u. of added vitamin D (Calciferol) per pint and 5 p.p.m. of iron. Specially suited for infants in first 3 or 4 months of life.

**Glax-Ovo** (*Glaxo Laboratories, London*). A tonic malted food beverage containing dried milk, chocolate malt extract, and 140 i.u. of Ostelin vitamin D per reconstituted pint.

**Hemolac** (*Cow & Gate, Guildford*). Full-cream milk powder containing 31½ gr. (0.45%) of iron and ammonium citrate to the lb. For prevention of anaemia in infancy.

**Lacidac** (*Cow & Gate, Guildford*). A dried milk with addition of 1 dr. of lactic acid B.P. to 1 pint of milk. Made in two strengths: Separated (1% fat) and Half-Cream (16% fat), the optimum dilutions being respectively 1 to 9 and 1 to 8 parts of boiled water. In convalescence, marasmus, eczema, diarrhoea and vomiting.

**Lacquin** (*Cow & Gate, Guildford*). Dried milk containing in 1 teaspoonful 2½ gr. of quinine. For use in the tropics.

**Lacto-Dextrin** (*Battle Creek Food Co., Battle Creek; Coates & Cooper, London*). A carbohydrate food with a high caloric value. Contains 73% of lactose and 25% of dextrin. For changing the intestinal flora, to combat auto-intoxication.

**Lactogen** (*Nestlé, London*). Dried cows' milk to which cream and lactose have been added.

**Mellin's Food** (*Mellin's Food, London*). A malted food in which all the carbohydrate has been rendered soluble.

**Neave's Food** (*Neave's Food, Fordingbridge*). A baked flour containing starch, to be made with milk and water. **Neave's Milk Food** is a dried milk with added lactose and maltose.

**Nestlé's Milk Food** (*Nestlé, London*). A mixture of desiccated Swiss milk, baked wheat flour and cane sugar (27%). Contains about 18% of starch.

**Ostermilk** (*Glaxo Laboratories, London*). No. 1 is a modified milk food enriched with 200 i.u. of vitamin D per reconstituted pint, and 5 p.p.m. of iron. Specially suited for use during the first few months of life. No. 2 is a full-cream milk food with fat and protein content unmodified. Contains 165 i.u. of vitamin D in each reconstituted pint, and 5 p.p.m. of iron. For the complete feeding of infants from the fourth month, the same as Full-Cream Glaxo.

**Ovaltine** (*Wander, London*). Composed of malt extract, milk, eggs and converted cocoa, and contains active lecithin. Analysis: Fat 8.01%, soluble carbohydrates 67.9%, nitrogenous substances as protein 14.2%, ash 3.76%, water 1.5%.

**Pantavene** (*Anglo-French Drug Co., London*). Tablets each containing 0.6 g. of total extract of the oat, *Avena sativa*. Advocated in debility, hypotension, etc. Dose.—2 tablets t.i.d.

**Peptalac** (*Cow & Gate, Guildford*). Pancreatised milk, dextrinised and pancratised wheat, retaining full mineral and vitamin content with freedom from pathogenic organisms. For use where powers of digestive tract are deficient.

**Plasmon** (*Plasmon, London*). Soluble casein. Nutritive and easily digested. Plasmon biscuits, arrowroot, cocoa and chocolate are prepared.



**Savory & Moore's Food** (*Savory & Moore, London*). Wheat flour with addition of malt, the carbohydrate being rendered soluble.

**Secway** (*Trufood, London*). Whey protein (chiefly lactalbumen) 13%, milk sugar 76%, milk salts 9%, fat and moisture of each 1%. In premature and delicate infants.

**Sister Laura' Food** (*Sister Laura's Food Co., Glasgow*). A starchy food to be added to undiluted milk.

**Soluble Protein G.L.** (*Glaxo Laboratories, London*). Soluble sodium salt of casein (protein 91.5%) for use in high protein feeding. Added to skim milk in the proportion of 20 gr. to 1 oz. In fermentative diarrhoea and to increase alkalinity of stools.

**Trufood** (*Trufood, London*). A dried milk without added sugar. Humanised Trufood is also available.

**Starchless Bread** (both brown and white) also biscuits and flour are manufactured. These are generally gluten products (more or less free from starch) and bran foods. Previously they were the only foods available for diabetics. Casein (with eggs and butter) has latterly been employed. Casein bread and biscuits (*Callard & Co., London*) are free from carbohydrates.

It is best to give this casein bread with a weighed quantity of starchy bread when desired. "Gluten bread" may contain as much as 55% of starch. It can be made with 7% of starch, but it is not palatable.

Almonds and other nuts are also used for making bread and biscuits. Various sugarless condiments, foods and drinks are prepared. Saccharin is used as the sweetening agent.

**Sugar-free Milk for Diabetics.** Prepared by a process of separating and washing with warm water, using a dairy cream centrifugal separator. Pour a gallon of cream into a 10-gallon can, fill with water at proper temperature for skimming, and thoroughly stir. Adjust separator to deliver 1 part out of the original 10. The cream is separated and the reservoir and separator bowl rinsed, while still running, by adding more warm water. On repeating the process the cream becomes sugar-free. Flavour restored by addition of salt (0.5 to 0.7%) and a little saccharin (added just before serving).

The following lists may be useful in assisting the SELECTION OF FOODS FOR DIABETICS:—

(i) Foods free from carbohydrates or containing less than 1%:—Beef, mutton, lamb, pork, poultry, game, sweetbread, tongue, fish, turtle, lobster, eggs, butter, Cheshire, American, Dutch and gorgonzola cheeses, lard, gelatin and starch and sugar-free special foods.

(ii) Foods containing a low proportion of carbohydrates (percentage of carbohydrate is indicated):—Liver 1, sausage (pork) 1, crab 1, crayfish 1, scallops 3, asparagus 3, celery 3, cucumbers 3, lettuce 3, spinach 3, oysters 4, mussels 4, stilton cheese 3, cheddar 4, rhubarb 4, tomatoes 4, mixed pickles 4, cauliflower 5, leeks 6, radishes 6, mushrooms 7, water melons 7.

(iii) Foods rich in carbohydrates:—Milk 5 or more, whey 5, oatmeal (thin gruel) 6, strawberries 7, turnips 8, carrots 9, beet (fresh), cranberries and pine-apple 10, oatmeal (boiled), blackberries, dried peaches 11, oranges 12, parsnips, apricots, currants, walnuts and filberts 13, apples and pears 14, macaroni (cooked) 16, calves foot jelly, artichokes, peas (green), cherries and almonds 17, potatoes and pears (dried) 18, figs and grapes 19, plums 20, boiled potatoes 21, bananas 22, rice (boiled) 24, tapioca pudding and cocoa-nuts 28, chocolate 30, mince pie 38, chestnuts (fresh) 42, apple pie 43, bread (brown) 47, potatoes (fried chips) 47, bread (white) 53, rolls 56, lentils (dried) 60, bread (toasted) 61, peas (dried) 62, gingerbread 63, macaroons 65, sponge cake 66, oatmeal 67, chestnuts (dried) 74, sago 78, tapioca 88, arrowroot 97, dried fruits, i.e., apples, apricots, currants, dates, figs, prunes, raisins 62 to 78, meal flour, rice, macaroni, vermicelli 70 to 80.

In the case of list (ii) much of the carbohydrates in some of them is in the form of cellulose, which is not absorbed.

The carbohydrate content of common British fruits and vegetables.—*Spec. Rep. Ser. med. Res. Coun., Lond., No. 135, 1929.*

## CEREVISIÆ FERMENTUM

*B.P.C.*

*Syn. FÆX MEDICINALIS (P. Jap. V).*

*Dose.*— $\frac{1}{2}$  to  $\frac{1}{2}$  ounce (8 to 16 g.) of compressed yeast;  $\frac{1}{2}$  to 1 drachm (2 to 4 g.) of dried yeast.

The cells and spores of *Saccharomyces Cerevisiæ*.

*P.G. VI* requires *Fæx Medicinalis* to be dried at a temperature not exceeding 40° and to retain its fermenting properties. Compressed and dried yeasts are included in *P. Helv. V. Fr. Cx.* specifies brewer's yeast, dried below 40° and powdered; it should have retained its vitamin B<sub>1</sub> content.

The chief species used in the fermentation industries are *Saccharomyces cerevisiæ*, *S. Carlsbergensis*, and *S. monacensis*. Brewer's yeast is a viscid frothy liquid with bitter taste. Baker's yeast or compressed distiller's yeast is obtained by filtering fermenting liquids and compressing the product. Dried yeast is prepared at temperatures not above 30°.

*Uses.* Fresh yeast may be useful in indigestion and flatulence. Both fresh yeast and the dried form are given to check boils and for acne. It is said that fresh yeast given *per os* grows actively in the stomach and slightly reduces sugar in diabetes. Yeast has been used for constipation, as also in tuberculous affections and in dysentery. In dyspepsia due to swallowing nasopharyngeal pus, it acts gastrically, and probably by *direct* contact. It not only checks vomiting, but after 14 to 21 days' use it will be noted that the patient loses the icteric complexion and gets a healthy colour.

Some hold the action of yeast is virtually that of nucleïn, as it is still effective after the yeast has been heated to 130° for an hour.

**YEAST EXTRACTS AS FOOD.** These have almost no caloric value. Their chief dietary value lies in their vitamin B content, and they are employed for this purpose both in the prevention and treatment of pellagra, beri-beri, and other vitamin B deficiency diseases. They are sometimes used to adulterate and enrich genuine meat extracts, which they resemble closely in taste. The chief chemical difference between the yeast and meat extracts is the presence of adenine in the former and creatine and creatinine in the latter.

*Extractum Fæcis (P.G. VI, P. Jap. V).*

Prepared by first removing the bitterness of fresh "lower" beer yeast with 1% sodium carbonate, and then submitting to a process of auto-digestion in the presence of hydrochloric acid, finally extracting the mass with water, evaporating and incorporating 25% of "medicinal yeast" (entire yeast with bitterness removed) to produce the powder. The extract is used as pill excipient.

**Tabellæ Cerevisiæ Fermenti (B.P.C.)** contain 5 gr. (0.3 g.) of dried yeast.

**Fæxalin (Coates & Cooper, London).** Dry beer-yeast in the form of flakes.

*Dose.*—A teaspoonful to a tablespoonful thrice daily with water, milk or wine.

**Fæxin** (*Martindale, London*). A dry powdered yeast. *Dose*.—One teaspoonful in water, beer or milk, with meals.

**Fæxin Extract** is made by extracting fresh yeast. Used for the various affections for which fresh and dried yeast is employed, e.g., in acne, erysipelas, furunculosis, folliculitis, leucorrhœa, diabetes, conjunctivitis, phlyctenulosa, typhoid and acute articular rheumatism. Available in pills and tablets containing 3 gr.

**Marmite** (*Marmite Food Extract Co., London*). A palatable yeast extract, rich in vitamin B complex. It is stated to promote growth in weakly children, and assimilation of fat; produces leucocytosis in chronic septic conditions and increases general metabolism. It is also of value in pellagra and polyneuritis, and in macrocytic anæmia and sprue.

Pernicious anæmia of pregnancy treated with Marmite and with liver extract. Both preparations are active even when the anæmia is complicated by malaria or hook-worm. Marmite thought equal to liver. Suggests that macrocytic anæmia is a deficiency disease.—Lucy Wills, *Brit. med. J.*, i/1931, 1059.

Two cases of megalocytic hyperchromic anæmia associated with tetany and steatorrhœa cured by Marmite, 12 g. daily. Marmite useless in the treatment of Addisonian pernicious anæmia. There is probably a factor common to both liver extract and Marmite, but its determination is not yet possible.—J. M. Vaughan and D. Hunter, *Lancet*, i/1932, 833.

Good results reported from its use in tropical macrocytic anæmia and sprue in India.—Lucy Wills, *Lancet*, i/1932, 838. See also Sir L. Rogers, *ibid.*, 906.

Marmite was found to be an effective alternative to liver extract in the treatment of pernicious anæmia, the hæmoglobin increasing more rapidly than the red blood count in Marmite treatment, while the converse was seen in liver treatment. Dosage was 3 tablespoonfuls per day for primary and relapsed cases, 3 teaspoonfuls for maintenance.—A. Goodall, *Lancet*, ii/1932, 781.

The response to treatment of anæmia with Marmite depends on the ability of the stomach to secrete an intrinsic factor. Thus Marmite was helpful in the cure of the macrocytic anæmia of sprue but not in Addisonian pernicious anæmia.—S. Davidson, *Brit. med. J.*, ii/1933, 481.

In their present form yeast or its products cannot be considered as substitutes for liver, liver extracts or gastric tissue products. The variation in response to treatment with yeast preparations can be explained by definite variations in the degree of failure in secretion of the intrinsic factor.—S. Davidson, *Med. Annu.*, 1935, 20.

**Mycolactine** (*Anglo-French Drug Co., London*). Combination of bile extract, yeast and lactic ferments. *Dose*.—2 tablets before each meal. Constipation, intestinal toxæmia, etc.

**Mycoosin** (*Richter, London*). Desiccated yeast tablets.

**Proliferase** (*Anglo-French Drug Co., London*). Suspension of living yeast cells—130 to 140 million cells per ampoule. In ampoules for oral administration in constipation, vitamin B deficiencies, furunculosis, etc.

**Simfax** (*Crookes Laboratories, London*). Pure standardised yeast.

**Penicillin**. During the growth of moulds a substance of unknown composition is formed, which has the power of inhibiting the growth of many bacteria. This substance is called penicillin, and it has been extracted as a solid mixed with coloured material. The purest extract so far obtained contains about 20% of penicillin. It has been tested against pathogenic organisms and found to be an extremely potent antiseptic even in high dilutions.

Hæmolytic streptococci were inhibited in a dilution of 1 in 800,000 of penicillin, as compared with 1 in 200,000 of sulphathiazole. Penicillin is apparently non-toxic.—A. Fleming, *Pharm. J.*, ii/1940, 172.

Penicillin is active *in vivo* against at least three of the organisms inhibited *in vitro*. It does not appear to be related to any chemotherapeutic substances at present in use and is particularly remarkable for its activity against the anaerobic organisms associated with gas gangrene.—E. Chain *et al.*, *Lancet*, ii/1940, 226.

Extracts of *B. Coli* were found to contain an enzyme (termed **penicillinase**), which destroyed the growth-inhibiting property of penicillin. It can be precipitated (with much loss of activity) by 2 volumes of alcohol, and its activity

increases considerably towards the alkaline range of pH. It is very active at pH 8 and 9; above the latter penicillin is unstable. Penicillinase was absent from extracts of *Staph. aureus*. The bacteriostatic action of the sulphonamide drugs is inhibited in the presence of tissue constituents and pus. Penicillin, not affected under these conditions, has thus a definite advantage. Since some bacteria contain an enzyme acting on penicillin, it is possible that the latter may have a function in their metabolism.—E. P. Abraham and E. Chain, *Nature, Lond.*, ii/1940, 837.

**Penicillin snuff**, containing penicillin 1, menthol 5, lycopodium 90, was tested on 4 subjects. It greatly decreased the number of staphylococci, although in 3 subjects the number increased again after treatment was stopped.—M. E. Delaheld *et al.*, *Brit. med. J.*, i/1941, 145.

### Vitamin E.

Vitamin E is an oil-soluble substance occurring in the oil from wheat-germ, rice-germ, cottonseed and maize, and in green leaves such as those of lettuce. Wheat-germ oil is the most commonly used source, and it should be stored at low temperature. The non-saponifiable fraction of this oil consists mainly of sitosterol, and when this is removed there remains a fraction having the characteristic physiological action of vitamin E. From this active fraction *alpha*-tocopherol, an alcohol of the empirical formula,  $C_{55}H_{100}O_2$ , has been isolated as a light yellow viscous oil insoluble in water, but soluble in alcohol and organic solvents, and found to have vitamin E activity to a marked degree. *Beta*-tocopherol and *gamma*-tocopherol have also been isolated from wheat-germ oil and from palm oil and cotton seed oil, but these two compounds have the biological activity of vitamin E in lesser degree than *alpha*-tocopherol.

**Uses.** Preparations of vitamin E are used in the treatment of patients with a history of habitual abortion. They are also used in cases of threatened abortion or premature separation of the placenta, and even in the later months success has been obtained. Vitamin E has been employed in the treatment of pregnancy toxæmia, and the routine administration of vitamin E to all pregnant women is recommended. Sterility treated by administration of vitamin E responds only if the condition is due to hypovitaminosis E, which is of rare occurrence. Muscular dystrophy has also been successfully treated by whole wheat-germ.

5 ml. wheat-germ oil each day for 2 weeks, then 5 ml. on alternate days for 2 weeks and subsequently 5 ml. every sixth day were given to each of 2 women who had had 4 and 5 consecutive miscarriages respectively; and each one then had a living child born.—P. Vøgt-Møller, *Lancet*, ii/1931, 182.

Doses of 40 drops of wheat-germ oil three times daily for 4 months (third to seventh month of pregnancy) followed by a dessertspoonful of wheat-germ three times a day were effective in curing 17 out of 20 cases of habitual abortion.—P. Vøgt-Møller, *Hospitalstidende*, 1933, 76, 621.

Use of vitamin E in 20 cases of habitual abortion and 5 of sterility. Successful in 17 cases of the habitual abortion group and in 2 of the sterility group. Treatment consisted in the administration of 40 drops of wheat-germ oil 3 times daily from the 3rd to the 7th month of pregnancy with a dessertspoonful of wheat-germ 3 times a day.—P. Vøgt-Møller, *Hospitalstidende*, 1933, 76, 621.

Nineteen successful pregnancies and 5 expectant cases (*i.e.*, patients were past the time when abortion usually occurred) out of 27 cases of habitual abortion treated with vitamin E. In 3 cases of threatened abortion similarly treated there were 2 successes and 1 failure. In all of 10 cases of sterility treatment was unsuccessful.—W. Pelton Tew, *Canad. med. Ass. J.*, ii/1934, 521.

Of 29 cases treated, 23 have been delivered and the other 6 are all past the sixth month of pregnancy, the average length of treatment being 5 months. The 23 delivered mothers had had collectively 73 previous pregnancies, resulting in the birth of only 11 living children, 5 of which died immediately after birth. Vitamin E was given in the form of wheat-germ oil, 1 3-minim capsule daily *per os*, together with vitamins A and D.—D. W. Currie, *Brit. med. J.*, i/1936, 752.

Thirty-seven women who had collectively 130 pregnancies gave birth to only 16 viable children. Under treatment with vitamin E in a dose of not less than 3 minims of the oil extract daily these women produced 37 living children. Two of them aborted, there were two sets of twins and 4 children died in hospital from prematurity.—David Currie, *Brit. med. J.*, ii/1937, 1218.

The necessity for vitamin E for normal embryonic growth in animals other than the rat and the mouse has not been established. It is difficult to obtain proof that vitamin E is of value in the treatment of habitual abortion in human beings.—F. J. Browne, *Proc. R. Soc. Med.*, 1939, 32, 863.

While there can be no conclusion on general grounds as to the indispensability of vitamin E to the human species, an analysis of the results obtained to date by various chemical workers affords at least presumptive evidence that it is needed for normal pregnancy in women.—A. L. Bacharach, *Brit. med. J.*, i/1940, 890.

**MUSCULAR DYSTROPHIES.** Of 18 cases of muscular dystrophy, chiefly in children, the results of treatment with vitamin E were remarkable. Every patient, except one, improved who was treated for more than six weeks, even bed-ridden patients showing improvements. When it is remembered that these cases should have got worse, or at least remained the same, such definite improvement must mean that this treatment promises success in a disease which has always, until now, been hopeless. The slowness, however, of recovery and the necessity for prolonged treatment must be emphasised. The results obtained support the contention that muscular dystrophy and amyotrophic lateral sclerosis are deficiency diseases and curable. The treatment consisted of the administration of  $\frac{1}{2}$  oz. of fresh dried whole wheat-germ twice daily over a prolonged period.—F. Bicknell, *Lancet*, i/1940, 10.

**Davitamon E** (*Organon Laboratories, London*). Capsules each containing 0.5 ml. of wheat-germ oil.

**Ephynal** (*Roche Products, Welwyn Garden City*). Tablets containing 3 mg. of synthetic  $\alpha$ -tocopherol acetate.

**Fertilol** (*Vitamins Ltd., London*). Brand of wheat-germ oil. *Dose*.—3 5-minim capsules daily for a minimum period of 3 months recommended.

**Germinal** (*Paines & Byrne, London*). Wheat-germ oil concentrate issued in 1 ml. ampoules containing the equivalent of 100 g. of wheat-germ, and in capsules containing the equivalent of 5 g. of wheat-germ oil.

**Phytoferol** (*British Drug Houses, London*). Capsules each containing 3 m. of oily concentrate equivalent in activity to 3 mg. of *dl*- $\alpha$ -tocopherol.

**Profecundin** (*Richter, London*). Concentrated vitamin E preparation in solution and tablets. *Dose*.—30 to 40 drops of solution (1% vitamin E) or 2 tablets (each containing 0.01 g. vitamin E) three times daily.

**Trigol** (*Abbott Laboratories, London*). Brand of wheat-germ oil.

**Wheat-Germ Oil (Collosol Brand)** (*British Colloids Ltd., London*). Wheat-germ oil in capsules containing 3 minims (0.2 g.), the vitamin E potency being 40 units as expressed on the Pacini-Linn scale (*i.e.*, 25 mg. daily is required to ensure a litter of rats in a vitamin-E-depleted mother).

**Viteolin Capsules** (*Glaxo Laboratories, London*). 3-minim capsules containing the unsaponifiable matter from 5 g. of wheat-germ oil.

15 cases of habitual abortion, treated with 1 capsule daily for 3–6 months. Successful in every case.—G. C. M. McGonigle, *per Nutr. Abstr. Rev.*, 1934–5, 4, 613.

**Zygon** (*Squibb, New York; Savory & Moore, London*). Wheat-germ oil. Also available in 3 m. capsules. *Dose*.—One teaspoonful or 6 capsules daily.

**Acidum Nucleicum** (*B.P.C.*). *Syn.* NUCLEIC ACID (*Fr. Cx.*). *Dose*.—1 to 5 grains (0.06 to 0.3 g.). 15 minims of a solution made with alkalis *q.s.*, *v. infra*, hypodermically. Much larger amounts have, however, been given.

Greyish- or yellowish-white powder prepared from yeast. It is **insoluble** in water except in the presence of alkalis, with which soluble salts are formed. Its solution is acid to litmus paper, and liberates  $\text{CO}_2$  from carbonates. Insoluble in alcohol and ether.

When nucleic acid is ordered for injection, give the equivalent in the form of sodium nucleate, the sodium nucleate being prepared from nucleic acid and a sufficiency of sodium carbonate to make it neutral to litmus. A 5% sodium nucleate solution is usually supplied when a saturated solution of nucleic acid is ordered for injection. Sodium nucleate solutions should be prepared with normal saline and a sufficiency of phenol for preservative purposes.

**Uses.** Usually in the form of the sodium salt in the treatment of influenza, pneumonia, scarlet fever and puerperal fever, also in tuberculosis. Injections cause an initial leucopenia, which is quickly followed by a marked leucocytosis.

Sodium nucleate solution 2 ml., containing 0.05 g. per ml., intramuscularly increases leucocyte count; found of value in influenza.

Apparently saved life in a case of imminent pneumonia. 2 ml. given every 4 hours. Should be tried in puerperal fever and other bacterial infections.—*Brit. med. J.*, i/1928, 52.

**LOBAR PNEUMONIA.** Sodium nucleate 0.1 g. intramuscularly, of value. It brings down the temperature within 48 hours—otherwise the dose is repeated. Sodium bicarbonate also given by mouth in  $\frac{1}{2}$  drachm doses every 4 hours in severe cases when the urine contains acetone.—*Brit. med. J. Epit.*, i/1927, 64.

In lobar pneumonia of an asthenic type in which leucocytes do not rise in number as the disease advances.—J. D. Comrie, *Prescriber*, i/1927, 390.

**SEPTICÆMIA**, where operation is requisite, treated by *B. coli* 50 millions and *streptococcus* 10 million 10 days and again 3 days before operation, and on the night preceding operation, 5 ml. of 5% sodium nucleate intramuscularly.—D. P. D. Wilkie, *Brit. med. J.*, ii/1931, 595.

**Sodii Nucleas.** *Syn.* SODIUM NUCLEINATE (*Fr. Cx.*).

**Dose** (of 5% w/v solution).—1 to 2 drachms (4 to 8 ml.) orally;  $\frac{1}{2}$  to  $\frac{1}{2}$  drachm (1 to 2 ml.) by injection.

Is used as a 5% solution obtained by treating nucleic acid with sufficient sodium carbonate to form a solution neutral to litmus.

**Nargol** (*Parke, Davis, London*) and **Cuprol** (*Parke, Davis, London*) are compounds of nucleic acid with respectively silver and copper. Cuprol is of use in granular ophthalmia in the form of 5% instillations. Nargol is soluble in water 1 in 4. Contains about 10% of Ag. It is supplied in the form of **Nargol Bougies**, 1% and 2%, for the treatment of specific urethritis.

**Acidum Thymicum.** *Syn. and Prop. Name.* NUCLEOTIN-PHOSPHORIC ACID, **SOLUROL** (*Allen & Hanburys, London*).

**Dose.**—4 to 6 grains (0.25 to 0.4 g.).

A yellowish-brown powder soluble in water. The solution dissolves uric acid, and has been used in the treatment of gout. It may also be administered by intramuscular injection in 2 gr. doses.

**Pentose Nucleotide.** Obtained by the alkaline hydrolysis of the nucleic acid of yeast by means of 1% sodium hydroxide. The resulting solution is acidified and the precipitated acids are purified by means of their lead salts, re-precipitated, and converted into the sodium salts. The latter are used therapeutically as an approximately 8% solution. The preparation probably contains the sodium salts of four nucleotides (compounds containing

phosphoric acid, pentose and pyrimidine radicals) of the general formula  $\begin{matrix} \text{HO} \\ \text{O} \diagup \text{P} - \text{O} - \text{C}_5\text{H}_8\text{O}_2 \cdot \text{B} \\ \text{HO} \diagdown \end{matrix}$ , where B is one of the bases guanine, adenine, cytosine or uracil, the pentose present being *d*-ribose.

**Uses.** The solution is given by intramuscular injection in doses of 10 ml. or more twice daily, in all cases exhibiting a leucopenia or neutropenia, especially in agranulocytic anæmia. This dosage is continued until an increase in the white cells is noted and is then reduced to 10 ml. daily, until a normal count has persisted for several days. In more severe cases 20 ml. twice a day for the first four days can be given. In successful cases the leucocyte count begins to return to normal about 5 days after treatment is commenced. In susceptible patients the injections may cause a temporary reaction accompanied by dyspnoea, bradycardia and sweating.

The standard dose is 10 ml., containing 0.7 g., administered intramuscularly twice daily till white cell count has risen definitely, and then once daily till count has been within normal limits for at least 3 days. Double the dose in desperately ill cases. If reactions occur (dyspnoea, precordial distress, sweating or vomiting) give divided doses into a site previously anaesthetised by Novocain and adrenaline. Description of a case successfully treated.—H. L. Marriott, *Lancet*, i/1934, 448.

In a series of 4 cases it was given in 1 acute case with benefit and in 3 chronic cases, with benefit in 1 and no effect in 2. In two other cases its use had to be abandoned owing to the severity of the reaction—one patient, who had previously been in a good condition, passed into a stuporous state and died. It will be agreed by those who have experience of Pentnucleotide that the reactions are not infrequently severe enough to prohibit further use of the drug. One reason that we have not been more fortunate in this country (as compared with America) may be insufficient dosage—in severe cases it seems desirable to inject 50 ml. a day. It is hoped that some means will be found to abolish the unpleasant side-actions of the drug so that doses of this order can be given with safety.—L. J. Witts, *Proc. R. Soc. Med.*, 1936, 29, 680.

An analysis of 393 cases recorded in the literature since 1933. The mortality in 75 untreated cases was 78%. The mortality in 43 cases receiving no specific therapy, but which received more than three days of general hospital care, was 70%. The mortality in 130 cases receiving inadequate amounts of any supposedly specific therapy was 77%. The mortality in 26 cases treated with adequate amounts of liver extract was 62%. The mortality in 85 cases treated with Pentnucleotide was 35%. At present it would appear that Pentnucleotide in doses of at least 40 ml. a day is the most promising form of specific therapy in this disease.—H. Jackson and T. J. J. Tighe, *New Engl. J. Med.*, i/1939, 732.

A patient with severe pulmonary tuberculosis and tuberculous laryngitis received sanatorium treatment and artificial pneumothorax. Following Sano-crysin therapy, agranulocytic anæmia developed, and was treated with Pentnucleotide. From one of the injections a staphylococcal abscess of the buttock developed, and this appeared to initiate recovery, which was eventually complete.—A. B. Taylor, *Lancet*, ii/1937, 74.

A case of pneumococcal peritonitis with leucopenia successfully treated with sodium pentose nucleotide.—J. B. G. Muir, *Brit. med. J.*, i/1938, 942.

**Liquor Nucleotidi.** The Committee on Pharmaceutical Chemistry of the Pharmacopœia Commission (*Report* 12) have recommended the inclusion in the B.P. of solution of pentose-nucleotides prepared by the hydrolysis of nucleic acid with a solution of sodium hydroxide, followed by purification of the nucleotides, and preserved with 0.3% of cresol.

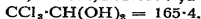
**Pentide** (Allen & Hanburys, London), **Pentnucleotide** (Syn. NUCLEOTIDE K. 96) (Smith, Kline & French, Philadelphia; Menley & James, London) and **S.P.N.** (Evans, Sons, Lescher & Webb, Liverpool) are preparations of sodium pentose nucleotides.

**Guanidine.** Treatment with guanidine hydrochloride caused a marked and well-sustained improvement in muscular function in 5 cases of myasthenia gravis without the presence of undesirable symptoms. The drug may be administered either intravenously (2% solution in normal saline) or orally in gelatin capsules, and is equally effective by either route. 10 mg. per Kg. is a safe and adequate amount to give as a single dose to test the effectiveness in a given individual. For continued medication the total daily dose and the times of administration of divided doses must be worked out in terms of the needs and tolerance of each patient. Compared with normal persons, patients with myasthenia gravis can tolerate larger doses of guanidine over an indefinite period without the production of hyperguanidinemia, the presence of which is indicated by gastro-intestinal or other symptoms. While these symptoms can be relieved by atropine they should serve as a warning that the administration of guanidine should be temporarily reduced or withheld. Treatment with guanidine may be combined with prostigmine.—A. S. Minot *et al.*, *J. Amer. med. Ass.*, ii/1939, 553.

**Adenine Sulphate.** Adenine sulphate, prepared by the hydrolysis of yeast nucleic acid, when given intravenously in 2 g. doses, is specific and non-toxic in stimulating myeloblastic activity in granulocytopenia developing as a result of severe sepsis. The material is prepared for injection by dissolving the salt in normal saline 1 g. to 100 ml. by boiling. It is not readily soluble, and it may be necessary to add 10% hydrochloric acid to the suspension for complete solution.—E. L. Richmond, *New Engl. J. Med.*, ii/1939, 267.

## CHLORAL HYDRAS

B.P., U.S.P. XI, *Fr. Cx.*, *P. Ned. V*, *P. Helv. V*, etc.



Syn. TRICHOETHYLIDENE GLYCOL.

[P1] "*Chloral hydrate.*"

**Dose.**—5 to 20 grains (0.3 to 1.2 g.) in aqueous solution or in chloroform water, well diluted. *P. Helv. V* and *P. Dan.* have max. single dose 45 grains, max. during 24 hours 90 grains. *Fr. Cx.* has 60 and 180 grains.

Colourless, non-deliquescent crystals, volatilising slowly in air. It liquefies at 50° to 58°.

**Soluble** 4 in 1 of water, 5 in 1 of alcohol, 2 in 1 of glycerin, 2 in 1 of ether, and 1 in 3 of chloroform, likewise soluble in oils and fats.

**Incompatible** with alkalis and alkaline salts (e.g., soluble barbitone), ammonium salts, borax, tannin, potassium iodide or permanganate, and with alcohol—chloral-alcoholate may separate. Liquefies with camphor, *q.v.*, and with quinine salts.

**Antidotes.** Empty stomach by emetic or by stomach tube, using at least 2 gallons of water at 105°F. Keep patient lying down and warm with hot blankets and hot-water bottles; he must be roused but *not* walked about. Give hot, strong coffee; aromatic spirit of ammonia,  $\frac{1}{2}$  dr. in 4 oz. of water. Caffeine sodium benzoate, 2 gr., and strychnine,  $\frac{1}{8}$  gr. hypodermically. Oxygen, or oxygen with 7% carbon dioxide, inhalations may be needed, also artificial respiration.



**Uses.** A hypnotic of special value in nervous insomnia, puerperal mania, insanity and delirium tremens. Small doses produce a sound natural sleep lasting for several hours. Its effect may be enhanced by the addition of morphine or bromide. It is also a valuable sedative against the convulsions of strychnine, tetanus and eclampsia, and has been employed in asthma and seasickness. Clinical trials show that chloral hydrate in therapeutic doses has no harmful effect on the heart. It is a remarkably effective hypnotic almost entirely free from habit formation. Its use is best avoided in the presence of gastro-intestinal irritation, though this drawback can be practically eliminated by diluting sufficiently with water. When the blood pressure is lowered during chloral hydrate administration, the effect is not much greater than occurs in natural sleep—actually many patients have an *increased* blood pressure after taking chloral hydrate.

It is used externally as an anodyne and counter-irritant in liniments for rheumatism, sciatica, etc.

Suppositories containing up to 33½% of chloral hydrate may be prepared by dissolving the medicament in the minimum quantity of water in a tared dish, adding sufficient melted oil of theobroma to produce the required weight and triturating with a glass pestle until homogeneous. A 15 gr. mould holds 17½ gr. of a suppository mass made in this way, equivalent to 5.8 gr. of chloral hydrate.—F. R. C. Bateson, *Pharm. J.*, 1936, 122.

**INFANTILE CONVULSIONS** controlled by 2 to 4 gr. *per os* or 5 grains *per rectum* repeated 2-hourly. When convulsions cease, gradually reduce dose to ½ gr. twice daily, then give calcium chloride 15 to 30 grains 4-hourly for 3 days.—*Per Lancet*, i/1932, 897.

[P1] **Chloral Camphoratum (B.P.C.).** *Syn.* PIGMENTUM CHLORAL ET CAMPHORÆ (T.H.), CHLORAL CUM CAMPHORA.

Chloral hydrate 1, camphor 1. (Measures 1½ by volume.)

It remains liquid at ordinary temperatures, and forms a valuable application painted on painful parts in neuralgia and rheumatism. It mixes freely with alcohol, ether, oils and fats, but not with water or glycerin. [D-P1-81] Cocaine 10% or less may be incorporated.

The compound (chloral and camphor) dissolves the alkaloids atropine, morphine and veratrine to the extent of 1 in 30 or more, but their salts are less soluble in it.

[P1] **Enema Chloralis Hydratis (B.P.C.).** *Dose.*—4 ounces (120 ml.). 1 to 3% w/v in mucilage of starch.

[P1] **Haust. Chloral. (N.I.F.).**

Chloral hydrate 20 gr., potassium bromide 30 gr., liquid extract of hyoscyamus 5 m., syrup 2 dr., water to 1½ oz.

[P1-81] **Liquor Bromidi Compositus (B.P.C.).** *Syn.* LIQUOR BROMOCHLORAL COMPOSITUS.

*Dose.*—½ to 2 drachms (2 to 8 ml.).

1 drachm contains 15 gr. each of chloral hydrate and potassium bromide with extract of cannabis and liquid extract of hyoscyamus.

Resembles [P1-81] **Bromidia (Battle & Co., St. Louis, Mo.; prepared in England by Roberts & Co., London)** which is stated to contain in each ounce chloral hydrate 91 gr., potassium bromide 91 gr., extracts of cannabis and of hyoscyamus 1 gr. each. *Dose.*—½ to 1 drachm in syrup or water.

[P1] **Lotio Chloralis Hydratis (Mid. H.).**

Chloral hydrate 10 gr., castor oil 30 m., alcohol (90%) 1 dr., water to 1 oz. For pityriasis capitis.

[P1] **Mist. Sedativa (P.M.H.).** *Syn.* TWO FIFTEENS MIXTURE.

Potassium bromide 15 gr., chloral hydrate 15 gr., peppermint water to 1 oz., for a dose.

[P1] **Mist. Sedativa c. Opio (P.M.H.).** *Syn.* THREE FIFTEENS MIXTURE.

Potassium bromide 15 gr., chloral hydrate 15 gr., tincture of opium 15 m., peppermint water to 1 oz., for a dose.

[P1] **Pigmentum Chloralis et Camphoræ Compositus (B.P.C.)** contains equal weights of chloral, camphor and phenol.

[P1] **Pigmentum Chloral Compositum.** *W.H.* has chloral hydrate 1, menthol 1, thymol 1, camphor 3. *R.D.H.* is the same, with name Linimentum Chloral Compositum. *L.H.* consists of equal parts of chloral hydrate, menthol and camphor.

[P1] **Syrupus Chloralis (B.P.C.).** *Dose.*— $\frac{1}{2}$  to 2 drachms (2 to 8 ml.).

Chloral hydrate and water *a.a.* 20% in syrup; 1 dr. contains about 11 gr.

**Somnos (Sharp & Dohme, London).** Elixir containing 5.5% of chloral glycerolate. Less depressing to the heart, circulation and respiration than chloral hydrate. *Dose.*—(*Sedative*) 1 or 2 teaspoonfuls in a glass of water; (*Hypnotic*).—1 or 2 tablespoonfuls. Infantile convulsions, colic, chorea, whooping cough, etc., and *per rectum* as hypnotic in post-operative cases and in spasmodic phillia.

**Chloralformamidum (B.P.C.).** *Syn.* CHLORALAMIDE.  
 $\text{CCl}_3\cdot\text{CH}(\text{OH})\cdot\text{NH}\cdot\text{COH} = 192.4.$

[P1] "*Chloral formamide.*"

*Dose.*—15 to 45 grains (1 to 3 g.) in weak spirituous or acidulated solution. Max. single dose 4 g., max. in 24 hours 8 g.

In colourless, odourless, shining crystals with a faintly bitter taste. **Soluble** 1 in 21 of water, 1 in 2 of alcohol, 1 in 12 of glycerin; readily soluble in ether and acetone. Hydrolyses when heated with water above 60°. M.p. 114° to 115° (*B.P.C.*), but commercial samples commonly melt at 118°. Incompatible with alkalis, giving chloroform, ammonia and a formate.

**Antidotes.** Treat as for poisoning by chloral hydrate.

**Uses.** Hypnotic in insomnia of alcoholism, neuralgia, hysteria, cardiac diseases and sea-sickness. It is slower and safer in action than chloral, into which it is probably decomposed. Chloralamide and potassium bromide of each 15 grains, with orange tincture and chloroform water has been recommended. It acts if given as an enema.

[P1] **Haust. Chloralamid. Co. (N.I.F.).**

Chloralformamide 20 gr., potassium bromide 15 gr., spirit of chloroform 20 m., water to 1½ oz.

[P1] **Chlorobrom (Burgoyne Burbidges, London).** *Dose.*— $\frac{1}{2}$  to 1 ounce. Contains 30 gr. each of chloralamide and potassium bromide in an ounce, flavoured with liquorice. For insomnia and sea-sickness.

**Butylchloralis Hydras (B.P.C.).** *Syn.* TRICHLOROBUTYLIDENE GLYCOL, CROTON-CHLORAL HYDRATE (formerly so-called).  
 $\text{CH}_3\cdot\text{CHCl}\cdot\text{CCl}_2\cdot\text{CH}(\text{OH})_2 = 193.4.$

[P1] "*Butyl chloral hydrate.*"

*Dose.*—5 to 20 grains (0.3 to 1.2 g.), in mixtures, pills or cachets.

This body is produced by the addition of water to liquid butyl-chloral, which is the final product of the action of chlorine on aldehyde. In pearly-white crystalline scales with pungent odour resembling that of chloral hydrate, and an acrid, nauseous taste.

**Soluble** 1 in 43 of cold water, 5 in 3 of alcohol 90% (forming an alcoholate), 1 in 20 of chloroform, 1 in 1 *w/w* of glycerin, 1 in 20 of olive oil and 1 in 2 of ether.

**Incompatible** with alcohol. Butylchloral alcoholate will be formed, and in case of some mixtures will be precipitated.

Menthol 2, with butylchloral hydrate 1 part, liquefy. Combines also with phenazone, *q.v.*

**Uses.** Hypnotic, but weaker than chloral and more depressing to the heart. Given for insomnia not due to pain. In combination with phenazone, cannabis or gelsemium, butylchloral is useful in migraine; neuralgia of nerves other than the cranial is rarely benefited.

[P1] **Mistura Butylchloralis.**

Butylchloral hydrate 4 grains, glycerin 15 minims, water to 1 ounce.

[P1-S1] **Pilula Butylchloralis cum Gelseminina.** NEURALGIC PILLS. Gelseminine hydrochloride  $\frac{1}{100}$  gr. (0.0003 g.), butylchloral hydrate 3 gr. (0.2 g.).

[P1-S1] **Tablets** are also prepared. For facial neuralgia 2 at the outset followed by 1 hourly until 6 have been taken.

[P1-S1] **Pilula Butylchloralis cum Camphora et Gelsemio.**

Butylchloral hydrate 2 gr., camphor 1 gr., alcoholic extract of gelsemium  $\frac{1}{2}$  gr., powdered acacia  $\frac{1}{2}$  gr., powdered tragacanth  $\frac{1}{2}$  gr., powdered liquorice 1 gr., syrup *q.s.* Varnish. Use similar to the last mentioned.

**Chlorbutol (B.P.).** *Syn. and Prop. Name.* ACETONE-CHLOROFORM (*P. Ital. V, Fr. Cx., F.E. VIII, P. Belg. IV*), ALCOHOL TRICHLOROISOBUTYLICUS (*P. Ned. V Supp. II*), CHLOROBUTANOL (*U.S.P. XI*), CHLORETONE (*Parke, Davis, London*).

**Dose.**—5 to 20 grains (0.3 to 1.2 g.) in cachet, capsule or tablet, followed by a draught of water or milk, or suspended in a mixture. *U.S.P. XI* average dose 10 grains.

It consists of trichloro-*tert.*-butyl alcohol,  $(CH_3)_3C(CCl_3) \cdot OH = 177.4$ , with a variable proportion of water of crystallisation. Samples usually contain about  $\frac{1}{2}H_2O$ . White crystals, with camphoraceous taste. The anhydrous substance has a m.p. of  $96^\circ$ ; the *B.P.* requires not lower than  $78^\circ$ . It volatilises with heat.

**Soluble** 1 in 125 of water, 1 in 10 of glycerin, 3 in 2 of alcohol 90%, 1 in 30 of liquid paraffin, 1 in 12 of olive oil; very soluble in ether and chloroform.

**Uses.** Chlorbutol is a local anæsthetic with an action weaker than cocaine, and an antiseptic with an action said to be fifteen times stronger than boric acid. Internally, it is hypnotic, and acts on the central nervous system similarly to chloral hydrate, but is less toxic and less irritant to the stomach.

Solutions in liquid paraffin 1 to 2% have been used for inflammation of the middle ear. Vaginal pruritus has been treated with a warm douche 0.4%. For piles, 5 grains in a 30 grain suppository; for a dusting powder for wounds and scalds use chlorbutol 23, with zinc oxide 120, and French chalk 90 parts. Capsules, 5 grains, check sea-sickness and other forms of vomiting, and are useful in whooping-cough, dysmenorrhœa, chorea and other spasmodic conditions.

**Antidotes.** Treat as for poisoning by chloral hydrate, *see p. 390*.

**TETANUS** successfully treated by chlorbutol in dose varying between 30 and 120 grains per rectum in olive oil and antitetanic serum. The chlorbutol injections reduce rigidity of the jaw.

**Narist. Chlorbutol.** (*N.I.F.*). Chlorbutol 5 gr., camphor 6 gr., oil of cinnamon 6 m., olive oil 2 dr., liquid paraffin to 1 oz.

**Nebula Chlorbutolis Composita** (*St. T. H.*). Chlorbutol 15 gr., camphor 40 gr., menthol 40 gr., oil of cinnamon 8 m., liquid paraffin to 3 oz.

**Solutio Chloretone Composita Inhalans.** *Syn.* SOLUCION DE CLORETONA COMPUESTA INHALANTE, *F.E. VIII.*

Chloretone 1 g., camphor 2.5 g., menthol 2.5 g., cinnamon oil 0.5 g., liquid paraffin 93.5 g.

**Boro-Chloretone** (*Parke, Davis, London*). Chloretone and boric acid. Antiseptic and analgesic dressing powder for use in eczema, urticaria, etc.

**Chloretone Inhalant** (*Parke, Davis, London*) contains Chloretone 1 g., menthol 1.8 g., camphor 2.5 g., oil of cinnamon *U.S.P. XI* (oil of cassia) 0.06 g., liquid paraffin to 100 g. A spray solution for use in catarrhal and congestive affections of nose, throat and bronchi.

**Chloretone Compound Ointment** (*Parke, Davis, London*). Chloretone, calomel, hydrastine, hamamelin, in lanolin and petrolatum base. For irritable and inflammatory conditions of the rectum.

**Dentalone** (*Parke, Davis, London*). Chloretone, oils of clove, cassia and wintergreen. Analgesic for treatment of painful and inflamed tooth sockets, etc.

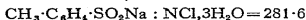
**Hæmamol** (*Duncan, Flockhart, London*). An astringent and anæsthetic ointment containing a small percentage of chlorbutol for use in hæmorrhoids. [**P1-S1**] **Hæmococones** (*Duncan, Flockhart, London*). Suppositories for use in conjunction with Hæmamol. Each contains morphine hydrochloride 0.2%, and procaine hydrochloride 1%.

**Mothersill's Remedy** (*Mothersill Remedy Co., London*) and **Zotos** (*Sangers, London*) contain chlorbutol—*cf. Proprietary Medicines*, Vol. II.

**Sedaform** (*Allen & Hanburys, London*). Chlorbutol capsules 5 grains.

## CHLORAMINA

*B.P., U.S.P. XI.*



*Syn. and Prop. Names.* CHLORAMINE-T, MIANIN (*P.G. VI, P. Belg. IV, F.E. VIII, P. Helv. V, P. Dan.*), CHLORAZENE (*Abbott Laboratories, London*), TOLAMINE (*Bürroughs Wellcome, London*), *p*-TOLUENE SODIUM SULPHO-CHLORAMIDE.

*Dose.*— $\frac{1}{2}$  to 3 grains (0.03 to 0.2 g.) has been given with charcoal.

**Solubility.** About 1 in 7 of water, 1 in 2 of boiling water, 1 in 7 of glycerin and 1 in 12 of alcohol. Organic solvents are undesirable. The aqueous solution is faintly alkaline and has a bitter taste. It is insoluble in liquid paraffin, ether, chloroform and benzene. It becomes less soluble on exposure to air, owing to decomposition.

**Incompatible** with alcohol, hydrogen peroxide and many other substances. Should not be mixed with other antiseptics.

**Uses.** For treatment of infected wounds and as a general surgical antiseptic, mouth-wash, vaginal douche and for urethral irrigation. It is non-irritant and practically non-toxic; does not coagulate blood serum. It has been used to replace Dakin's solution. Not suitable for intravenous use—has marked hæmolytic

action. 2% is used for infected wounds—increased to 4%. Mouth-wash, nasal or vaginal douche or for urethral irrigation (e.g., in gonorrhœa), 0.25 to 0.5%.

To sterilise water 1 in 250,000 is effective if a little citric acid (0.8 g. per litre) is added—the resulting water is not unpleasant to taste.

**Carbasus Chloraminæ** (B.P.C.) contains from 4 to 6% of chloramine. A 35% gauze is also made—the former for general use; the latter as preliminary dressing of a wound.

Use dry and subsequently moisten if necessary when in position.

**Chloramine Ointment.** *Syn.* ANTI-GAS OINTMENT No. 2. Anti-gas ointment for casualty services. Contains chloramine in a vanishing cream basis. Effective against mustard gas and lewisite. Speedy application is necessary, and it should be rubbed in for at least one minute. Also used as a prophylactic. Supplied in 1 and 4 oz. amber-coloured pots, fitted with air-tight closures.

**Lotio Chloraminæ** (I.H.). Chloramine 9 gr., normal saline solution to 1 oz. **Antipart** (Riddell Products, London). Foaming contraceptive tablet containing chloramine and saponin.

**Zonitors Chloramine Pessaries** (Fassett & Johnson, London). Contain sodium stearate 6%, potassium stearate 2.5%, hydrogen stearate 0.25%, chloramine 2%, water 89.25%. Contraceptive; also for leucorrhœa, vaginitis, etc.

**Dygerma** (Matthews Laboratories, Clifton, Bristol). A stabilised solution of chloramine in the proportion of 5% by weight. The chloramine is held in stable solution by the buffering action of the ions of sodium, potassium, and boron, and retains its activity for many years. It is a non-irritant and non-toxic germicide, miscible with water and readily diffusible. It does not exert a corrosive action even when used undiluted, and does not coagulate or precipitate proteins or retard the formation of granulation tissue. For use as a general antiseptic in surgery.

**Dichloramina** (B.P.C., F.E. VIII, U.S.P. XI). *Syn.* DI-CHLORAMINE-T, TOLUENE-SULPHODICHLORAMIDE.  
 $\text{CH}_3\cdot\text{C}_6\text{H}_4\cdot\text{SO}_2\cdot\text{NCl}_2 = 240.04$ .

Yellow crystals or crystalline powder with odour resembling chlorine. Decomposes on exposure to air with evolution of chlorine. M.p. about 78°.

**Soluble** 1 in 1 of chloroform, 1 in 1 of benzene, 1 in 3 of carbon tetrachloride, glacial acetic acid, chlorinated paraffin or eucalyptol.

This substance enables an oily solution to be prepared, the corresponding monochloride being insoluble in oils.

**Uses.** Is much more germicidal than chloramine and results are as good as with Dakin's solution. It has the disadvantage, however, of causing painful smarting when applied to open wounds, and of causing dressings to adhere to the wounds. In solution in chlorinated liquid paraffin, or in a mixture of chlorinated paraffin 1 and chlorinated eucalyptol 4, it is used as a disinfectant of the nasopharynx, e.g., in the treatment of meningococcus carriers (1 to 2% solution). 5% solutions may be applied as a spray to wounds, covering with gauze and re-dressing every 24 hours. Solutions are unstable, and should not be kept for more

than 2 to 3 days; they must not be used when a precipitate has appeared.

**Chlorinated Eucalyptol.**

Treat eucalyptol 100 ml. with potassium chlorate 3 g. and hydrochloric acid (conc.) 10 ml. for 12 hours or longer. Then wash with water and with sodium carbonate solution. Remove the water, add sodium carbonate 3 g., and allow to stand 24 hours. Filter and dry with a little calcium chloride.

**Chlorinated Paraffin.** *Syn.* CHLORCOSANE (*U.S.P.* XI).

A colourless or yellowish oil, slightly soluble in alcohol, miscible with ether, chloroform and benzene. May be prepared by treating liquid paraffin 20 parts with potassium chlorate 0.1 part and hydrochloric acid 0.5 part, in a wide-mouthed glass bottle, and allowing the mixture to stand until chlorine ceases to be evolved; the mixture is placed in direct sunlight until the odour of chlorine and the yellow colour of the chlorinated oil have disappeared, and is then shaken in a separator with a slight excess of sodium carbonate solution; the chlorinated product is separated, washed with water until free from alkali, and dried by means of anhydrous calcium chloride.

**Halazone.** *Syn.* *p*-SULPHONDICHLOROAMINO BENZOIC ACID.

$C_6H_4(SO_2 \cdot NCl_2) \cdot COOH = 270.0$ .

A white powder with a strong odour of chlorine. 1 in 300,000 is sufficient to sterilise ordinarily contaminated water in 30 minutes.

**Soluble** sparingly in water, insoluble in chloroform and petroleum. Soluble also in excess of cold sodium hydroxide solution, but with less quantity or with feebly alkaline salts, *e.g.*, phosphates or borates, hydrolysis occurs.

**Tablets.** To prepare, powder the acid 4, with dry sodium chloride 92 and add dried sodium carbonate 4 (or dried borax 8%). Pass through a No. 40 sieve (no lubricant required or indeed is to be used), and compress into tablets weighing 100 mg.

Each tablet so made contains 4 mg. of the disinfectant—sufficient for a litre or a quart of water.

**Gynomin** (formerly known as **Speton**) **Tablets** (*Coates & Cooper, London*). Contraceptive tablets containing sodium bicarbonate, tartaric acid, and sodium dichlorosulphamino-benzoate.

**Azochloramid.** A bright yellow, crystalline substance obtained by the chlorination of azodicarbonamidine, and containing about 98% of  $N,N$ -dichloroazodicarbonamidine,  $H_2N(CIN) : C \cdot N : N \cdot C : (NCl)NH_2$ . It has a chlorine-like odour and a burning taste; it explodes without melting at  $155^\circ$ . Slightly soluble in water, chloroform, ether and glycerin; soluble in alcohol; partly soluble in glacial acetic acid, acetone and ethyl acetate; solutions decompose on exposure to light.

Azochloramid is stated to be more effective for the dressing, packing or irrigation of wounds, cuts, etc., than chloramine or dichloramine. It is used as a 1 in 500 solution in glycerin triacetate or as 1 in 1600 and 1 in 3300 solutions in isotonic buffered saline solutions.

Azochloramid is active in such low concentrations that its toxic effects are negligible. Serum does not seriously interfere with its activity.—A. Winkler, *per Brit. chem. Abstr. B.*, 1939, 33, 1879.

**Azochloramid Solution in Triacetin** (*Wallace & Tiernan, London*). 1 in 500. Use undiluted as a wet dressing, packing or instillation. It should not be used on mucous membranes.

**CHLORINUM**

Cl = 35.46.

**Liquor Chlori (B.P.C.).** *Syn.* AQUA CHLORI. An aqueous solution of about 0.5% w/v of chlorine gas.

**Acidum Hypochlorosum.** HClO = 52.46. Hypochlorous acid, as such, has not been isolated. In solution and especially in the form of its salts—the hypochlorites, *e.g.*, those of calcium and sodium—it has played an important part in many chemical processes.

The acid in dilute solution is practically colourless; in a concentrated form it is yellowish. It readily undergoes decomposition with formation of chlorine, chloric acid, oxygen and water. It is hence a strong oxidising agent and for this reason a bleaching agent.

The hypochlorites have been extensively employed for wound treatment, as described in the following pages.

**Calx Chlorinata (B.P., P. Dan.).** *Syn.* SEL DE JAVELLE, CALCIUM HYPOCHLOROSUM CRUDUM (*Fr. Cx.*), CALCARIA CHLORATA (*P. Helv. V, P. Jap. V*).

Bleaching powder is a dull white powder containing not less than 30% of available chlorine.

**Uses.** Bleaching powder is a powerful disinfectant and deodorant, and is used to disinfect fæces, urine, and sanitary utensils. It may be used to purify water for drinking purposes in the proportion of 1 ounce to 2000 gallons; the taste may be removed by a few crystals of sodium thiosulphate.

It is frequently used for the removal of dyes from the skin of the hands and may cause irritation; to avoid this the hands, after using the powder, should be dipped in a 10% solution of sodium bisulphite and then rinsed with water.

**“Tropical” Bleaching Powder** is remarkably stable even in hot climates. It consists of bleaching powder with an excess of unslaked lime.

**Bleach Cream.** Tropical bleaching powder 3 parts, water 5 parts, by weight.

**Preparation.** Place the water in an earthenware or enamelled iron pail and add the powder slowly in four equal portions at intervals of one hour, stirring well after each addition with a wooden pole. Allow the mixture to stand for 24 hours, again stir well and allow to stand for a further 24 hours. No further setting takes place, and after remixing, the cream is ready for use. In an emergency, add all the powder to the water at once and stir well, repeating the stirring frequently during use. For emergency application to mustard gas burns.

A cream, made to this formula, will be available for free distribution at all pharmacies, in districts contaminated by mustard gas, whose proprietors co-operate in a scheme prepared by the Ministry of Home Security. Tropical bleaching powder and 2-gallon pails with lids will be supplied by the local authority, and, on receipt of instructions, pharmacists will prepare the cream and place the pails outside the pharmacy. 6 lb. of powder and 10 lb. of water suffice for a 2-gallon pail, and the cream will keep for about six weeks.

**Liquor Calcis Chlorinatæ (B.P.C.).** 10%. Contains not less than 2% w/v available chlorine, 3% when freshly made.

Is of great value as a spray in acute tonsillitis.

**Liquor Calcis Chlorinatæ cum Acido Borico (B.P.C.).**

*Syn.* EUSOL, LIQUOR ACIDI HYPOCHLOROSI COMPOSITUS.

This solution contains when freshly prepared about 0.4% w/v of available chlorine, but rapidly loses strength.

**Uses.** Eusol is employed as a general antiseptic in the form of a lotion or on gauze wrung out and applied without waterproof; or as a bath, full strength or diluted. The object is to secure the maximum effect with minimum irritation. As a lotion it should be used *warm*. It has no harmful effect upon the tissues, the effect being purely local. Flow of lymph is induced by it from the tissues. It removes offensive odour in a wound. For field use the antiseptic may also be employed in the form of dry powder if water is not available—*vide* eupad.

Has been used undiluted in injuries to the head or hands, lacerated, contused or incised, including cases which are septic, in mastoid operations and in cases of cerebellar abscesses, also for treatment of ulcers of the leg, gangrene of the feet, pyorrhœa alveolaris and follicular tonsillitis. In a wound superficial bleaching may occur with some irritation. If pain is produced, the application should be diluted with saline. Also used in cystitis by irrigation with 1 in 8 dilution, and in tuberculous lesions, streptococcal infections and gonorrhœa (1 in 5 dilution). It must not be applied for long periods to wounds of the back of the hand, dorsum of foot and of the neck, forearm and wrist. In general it should be applied once or, exceptionally, twice daily and should not be covered by protective. It should not be more than 3 weeks old.

**TONSILLITIS.** Eusol solution, 1 in 3, or 1 in 4, the most effective of all gargles for tonsillitis; used hourly.—H. L. Marriott, *Brit. med. J.*, i/1934, 104.

**Lot. Eusol (N.I.F.).** Dissolve boric acid 52 gr., in water and make up to 6 oz. Dilute this solution with 2 oz. of water, add chlorinated lime 50 gr., shake occasionally for 10 minutes, filter and make up to the required volume with water. It should be freshly prepared.

**Eupad. *Syn.* PULVIS CALCIS CHLORINATÆ ET ACIDI BORICI.**

Mix intimately equal weights of finely ground bleaching powder (dry) and powdered boric acid. Should be kept in stoppered bottles and not exposed to the light; in preference mix freshly. Contains about 15% of available chlorine.

**Caution.** The evolution of chlorinated vapour in mixing the ingredients is sufficient to "gas" the unwary.

**Uses.** Employed as a dry dressing for wounds. It evolves hypochlorous acid rapidly when moistened between layers of gauze or lint (as in the pad of a first field dressing) and covered with wool and a bandage. When applied covered with waterproof it should be used for a short time only—10 to 15 minutes as a rule. If it causes pain a weaker application is indicated. 1 to 2 g. is suitable in the first field dressing.

**Unguentum Calcis Chlorinatæ.**

A useful application for chilblains. 10% in paraffin ointment.

**Bleach Ointment. *Syn.* ANTI-GAS OINTMENT No. 1.** Anti-gas ointment for casualty services. For application to cases which



have been in contact with liquid mustard gas. To be rubbed in within three minutes of exposure and wiped off after one minute.

A **British Standards Specification (BS/ARP/40—1940)** has been issued for Bleach Ointment (Anti-gas Ointment No. 1). The specification requires that the ointment shall consist of equal parts by weight of bleaching powder and white mineral jelly, and shall contain not less than 14% of available chlorine immediately after preparation. The label of the containers must bear the following particulars:—(a) Bleach Ointment (Anti-gas Ointment No. 1), (b) the name of the maker, and (c) the date of manufacture.

Bleach ointment of yellow paraffin and bleaching powder is liable to explode during manufacture.—*Pharm. J.*, ii/1938, 383.

The following precautions should be observed to prevent the spontaneous overheating of bleach ointment during, or soon after, manufacture. A soft paraffin of low reactivity should be used; no heat should be utilised; after preparation the ointment should be rapidly filled into small receptacles, which should be freely exposed to the cooling action of the air; if it is inconvenient to divide the bulk of the ointment it should be prepared in or transferred to a shallow uncovered container for one or two days to encourage the dissipation of any heat which is developed, and as cool a place as possible should be selected for the manufacture and storage of the ointment, particularly during the first two or three days after preparation.—H. Brindle and L. V. Rosser, *Quart. J. Pharm.*, 1940, 265.

A satisfactory bleach ointment is obtained from chlorinated lime 50 g., calcium hydroxide 1.5 g., white soft paraffin 50 g. Melt the white soft paraffin and add the calcium hydroxide. Continue to heat with constant stirring. Strain and stir until *cold*. Triturate the chlorinated lime, previously passed through a No. 60 sieve, with a portion of the base. Gradually add the remainder, mixing thoroughly by trituration.—H. W. Tomsik, *Pharm. J.*, ii/1939, 447.

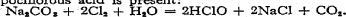
Samples of bleach ointment made with equal parts of tropical bleach (available chlorine 35 to 37%) and white soft paraffin, contained 16 to 17% of chlorine if the soft paraffin was of B.P. quality, but less (14 to 15%) if it was an inferior grade. On storage the loss of chlorine was rapid in the first few days, but gradually decreased, and samples tested after three months still contained 11% of chlorine.—A. G. Fishburn, *Pharm. J.*, i/1940, 35.

It is considered that a purchaser of bleach ointment for A.R.P. purposes is entitled to receive an article containing about 15% of available chlorine. It has been shown that in every instance when such an article has been sold, it has retained a high proportion of the active ingredient over a period of months, and that subsequent deterioration is likely to be very slow.—D. D. Moir, *Analyst*, 1940, 158.

**Liquor Sodæ Chlorinatæ (B.P.C.). Dose.**—10 to 20 minims (0.6 to 1.2 ml.). Contains 2.5 to 3% *w/v* of available chlorine. *Should be freshly made.*

Formerly used as an antiseptic for wounds and ulcers diluted with 15 to 60 times its volume of water. It is strongly alkaline and Liquor Sodæ Chlorinatæ Chirurgicæ (B.P.) is now preferred for medicinal purposes. For carbuncles Liquor Sodæ Chlorinatæ, diluted 1 in 20 or 1 in 30, is a non-irritant and effective dressing.

**Eau de Labarraque or Liqueur de Labarraque (Fr. Cx.)** is about  $\frac{1}{2}$  the strength of Liquor Sodæ Chlorinatæ (B.P.C.). Initially Labarraque made his bleaching solution by passing chlorine into sodium carbonate solution. In this case free hypochlorous acid is present:



**Eau de Javelle** (first made in 1789) was originally a solution of chlorinated potash made with potassium carbonate on the same lines as chlorinated soda solution, but it is now replaced in great measure by the soda compound.

**Cataplasma Sodæ Chlorinatæ (B.P.C.).** Linseed poultice prepared with a mixture of solution of chlorinated soda and an equal volume of water.

**Liquor Sodæ Chlorinatæ Chirurgicæ (B.P.).** *Syn.* DAKIN'S SOLUTION.

Prepared from chlorinated lime, sodium carbonate and boric acid, the proportions varying with the amount of available chlorine in the chlorinated lime. Contains from 0.5% to 0.55% *w/v* of available chlorine. The pH is about 9.5 and the solution is stable for about 3 to 4 weeks. The formula is based on a paper by H. Davis (*Quart. J. Pharm.*, 1931, 360).

**Uses.** A non-irritating antiseptic for wounds. Fresh quantities should be brought in contact frequently. The solution assists in the dissolution of necrosed tissue, forming soluble chloramines.

Liquor Sodæ Chlorinatæ (B.P.C.), owing to hydrolysis, gives rise to alkalinity, which increases with dilution, hence the boric acid was added with a view to neutralising the caustic alkali as formed.

The solution was first used by *Carrel's Method* (*Brit. med. J.*, ii/1915, 318), employing rubber tubes with holes throughout their length about 1 cm. apart. Pieces of gauze are placed round and between the tubes, and the solution runs into the wound and irrigates it. Soft paraffin is smeared on the surrounding skin. Cicatrisation is not delayed even by continuous use.

Diluted with 15 to 60 times its volume of water or normal saline it is used as a vaginal douche, for irrigating the bladder and as a mouth-wash. Locally in skin affections 10% to 30% dilutions may be used. *It must not be injected intravenously.*

Concentrated, stable solutions may be prepared by saturating 1 litre of 10% sodium hydroxide solution with boric acid and adding 3 g. of aluminium chloride. Chlorine is then passed in until the precipitation of magnesium hydroxide begins and it is then filtered.—L. Mellersh-Jackson, *per J. Soc. chem. Ind., Lond.*, 1938, 1295.

In the last war, possibly the most popular antiseptic for use in septic wounds was Dakin's solution, especially when it was used by Carrel's method of instillation into the wound through a manifold of tubes once every two hours. I have made observations (1919) as to how long Dakin's fluid maintains its antiseptic power in a septic wound. A cup-shaped wound was chosen, into which a measured volume of fluid could be introduced and removed. When Dakin's fluid was introduced and removed after ten minutes, it was found on testing the available chlorine that this had been reduced to a point below that which was antiseptic in serum. If the fluid was kept agitated during its sojourn in the wound, the strength was reduced below the antiseptic level in five minutes. Therefore, in Carrel's method, which was generally regarded as the most successful "antiseptic" treatment in the war of 1914-1918, there was an antiseptic in the wound for at the most, ten minutes out of every two hours.

It seems likely that the benefits obtained by the intermittent instillation of Dakin's fluid into a wound depend more on its physiological effect (drainage of the infected walls of a wound) than on any direct antiseptic action.—A. Fleming, *Proc. R. Soc. Med.*, 1940, 33, 487.

**OIL DERMATITIS** is emphatically preventable by the use of an alkaline lotion, e.g., *Liq. Sodæ Chlorinatæ* c. *Acid. Boric.*, as now used in many large engineering works.—W. J. O'Donovan, *Brit. med. J.*, ii/1932, 293.

One of the most common causes of dermatitis is the lubricating oil used in engineering, which gives rise to an acneiform condition. The use of Dakin's solution is a valuable preventive, and buckets of this placed in the wash-places or the shops for immersion of the hands prior to washing, or before commencing work, has reduced the incidence.—J. C. Bridge, *Brit. med. J.*, ii/1933, 326.

**Liquor Sodii Hypochloritis (U.S.P. XI).**

A solution of sodium hypochlorite, 4 to 6% NaOCl, which is not suitable for application to wounds.

**Liquor Sodii Hypochloritis Dilutus (U.S.P. XI).**

A modified Dakin's solution prepared by diluting Liquor Sodii Hypochloritis with water, adding sufficient sodium bicarbonate to produce a solution which is no longer alkaline to phenolphthalein, assaying and diluting to contain 0.48% w/v of NaOCl.

**Liquor Sodæ Chlorinatæ cum Sodii Bicarbonate (B.P.C.).**

*Syn.* DAUFRESNE'S SOLUTION. Contains about 0.45% w/v of available chlorine. **Chlorisol** (*Allen & Hanburys, London*). Concentrated hypochlorite solution for producing Dakin's solution.

**Fecto** (*Parke, Davis, London*). Alkaline solution of hypochlorites containing 4% of available chlorine. Disinfectant, deodorant and bleaching agent. Gargle in cases of diphtheria, etc.

**"Milton" Disinfectant** (*Milton Proprietary, London*). Contains sodium hypochlorite 1.01% with sodium chloride 16.8% and small quantities of chlorate, sulphate and carbonate, and calcium chloride. A deodoriser, preservative, insecticide and general antiseptic. It is stated to be harmless to the human system either internally or externally.

It is used for wounds and skin affections, either full strength or diluted down to 1 in 50 or more. For abscesses, fistulas, etc., it can be used undiluted. For the vagina and cervix 1 in 4. Dentures may be cleaned with it by the use of 10 to 20 drops—not more—in a tumbler of cold water overnight.

**CHLOROFORMUM**

*B.P., U.S.P. XI, P. Helv. V, Fr. Cx., etc.*

$\text{CHCl}_3 = 119.4.$

*Syn.* TRICHLOROMETHANE, FORMYL TERCHLORIDE, CHLOROFORMIUM AD NARCOSIN.

[P1] "*Chloroform.*"

[83] "*Chloroform—in substances containing less than 10% of chloroform.*"

*Dose.*—1 to 5 minims (0.06 to 0.3 ml.), in mucilage and water, or in a perle; 3 drops = 1 minim. Small doses may be given as chloroform water or spirit of chloroform. Very large amounts (up to 2 ounces) have been taken internally without causing death.

Chloroform has sp. gr. 1.485 to 1.490. About 15% v/v distils below 60°, the remainder at 60° to 62°. Should be kept in amber-coloured, stoppered bottles or in the dark.

**Soluble** about 1 in 200 of water; miscible with alcohol, ether, fixed and volatile oils, and most organic solvents.

**Antidotes** (for poisoning by drinking chloroform). Empty stomach by emetic or stomach tube. Give water freely, with 1 dr. of sodium bicarbonate dissolved in 1 pint. Keep patient lying down. Artificial respiration. Oxygen inhalations. Give 1 oz. of dextrose in 1 pint of hot strong coffee by rectum. No fats for some days; dextrose freely. For treatment of dangerous symptoms arising during anaesthesia, see below.

**Uses.** Inhaled, it is anæsthetic and analgesic. Brief inhalations may be used in angina pectoris and in croup. Internally is antispasmodic and sedative for asthma, colic, cough and neuralgia.

In sea-sickness, 1 or 2 drops of chloroform on a lump of sugar or in a wine-glass of iced soda water, repeated every 15 minutes, often give relief.

Externally in liniments to promote absorption and allay pain, as in neuralgia and sciatica. It may be used as a local anæsthetic for toothache, the tooth being plugged with a piece of cotton wool soaked in chloroform. A 20 to 30% chloroform ointment is effective against all forms of external parasitic infection.

1 in 500 is a preservative of infusions and animal extracts. It is a useful deodorant, *e.g.*, for the hands after post-mortem work.

Infection by intestinal parasites, *e.g.*, *Ankylostoma*, *Ascarides* and *Oxiurides* are well treated by doses *per os* of 3 to 4 g. mixed with castor oil or olive oil.

### ANÆSTHETIC USES OF CHLOROFORM

**Advantages of Chloroform.** (1) It is less irritating than ether vapour and its action is much more rapid. (2) The vapour is not explosive; chloroform can be used when a diathermy needle or cautery is to be employed. (3) It induces the most profound anæsthesia and relaxation. (4) It produces less suffocation, less excitement and less post-operative nausea and vomiting than ether.

**Contraindications.** The use of chloroform is not justifiable (1) in cases of grave debility with low blood pressure, especially in cases of patients suffering from shock; (2) in cases likely to develop acidosis, *e.g.*, the diabetic, the sufferer from septic abdomen, and children (especially in the presence of acute sepsis); (3) in a great many cases during the induction period. Chloroform should not be used as an anæsthetic in women at the menopause, in advanced heart disease, Graves' disease or hæmorrhage.

**Dangers.** Chloroform is far more dangerous than ether or nitrous oxide. The dangerous effects fall into five groups: (1) depression of the respiratory centre, (2) fall in blood pressure, (3) late toxic effects, (4) chloroform syncope, (5) possible damage to the eyes.

**ACTION ON THE LIVER.** Half-an-hour's administration of chloroform caused injury requiring 8 days for recovery. Ether produced definite but transitory effect and nitrous oxide and ethylene none, except with concomitant anoxæmia. —Wesley Bourne, Sect. of Anæsthetics, B.M.A. Cent. Meeting 1932, *Brit. med. J.*, ii/1932, 319.

**ACTION ON THE HEART.** Chloroform is a cardiac poison and investigations show that the patient under light chloroform anæsthesia is often in a precarious condition. Undesirable effects on cardiac rhythm are less likely if it is not given to patients who are fatigued, if it is preceded by an injection of morphine and atropine, or if it is administered in the sitting posture or with the head and shoulders raised. —Per *Lancet*, i/1932, 1208. See also E. F. Hill, *ibid.*, 1280.

**EYE TROUBLES** following anæsthesia. Acute conjunctivitis may be caused by vapour of chloroform or ether, and keratitis with subsequent corneal scarring may occur. Instillation of castor oil prior to anæsthesia, or irrigation with boric acid lotion afterwards, recommended as preventive measures. Keep lids carefully closed and avoid frequent examination. —J. Blomfield, per *Prescriber*, 1926, 142.

**Delayed Chloroform Poisoning** occasionally occurs after

recovery from the anæsthetic. Vomiting may persist, or may commence a day or two after the operation; other symptoms are headache, ketosis, scanty albuminous urine, and jaundice due to fatty degeneration of the liver. Pre-operative starvation and purgation, sepsis and long exposure to the vapour predispose to the condition which usually ends in coma and death. The administration of dextrose before the operation is the chief preventive measure. If the condition arises, administration of dextrose either *per os* or intravenously, together with insulin, may be successful if used early.

**Antidotes for treatment if dangerous symptoms arise during inhalation of chloroform.** Pull out tongue with forceps, remove mucus, etc., from mouth; loosen clothing, begin artificial respiration at once and keep it up for at least an hour. The inhalation of carbon dioxide and the intravenous injection of lobeline stimulate the respiratory centre. Keep patient warm and lying down with head well below level of body. Place hot flannels over heart and flap face and chest with the end of a towel. Strychnine,  $\frac{1}{2}$  gr., or caffeine sodium benzoate, 2 gr., hypodermically. Heart massage by subdiaphragmatic route.

Reported differences in the action of atropine on the heart in secondary chloroform syncope have been due to differences in mode of injection. It has been injected directly into the heart successfully, in contrast to results reported following injections into the jugular vein.—*C.R. Soc. Biol.*, Paris, 1935, 118, 854.

**Administration.** Chloroform is usually administered by a drop-bottle, using the open mask method (*vide* Ether). During administration the respiration and pulse should be carefully watched for signs of failure, and the operation should never be begun till the stage of muscular relaxation has commenced. For induction, the requisite concentration of chloroform vapour is about 2 to 3%, and the mask is held about an inch from the face. The anæsthetic is added slowly at first, the rate being gradually increased until about 30 to 60 drops per minute is being given, after which it is reduced as required. It is advantageous to ensure regular breathing of a proper depth by giving carbon dioxide and oxygen, the mask being placed on the face. Anæsthesia may be maintained by the drop method or, better, by some apparatus such as the Junker bottle, care being taken to see that the bottle connections are correctly made so that the patient receives chloroform vapour and not the liquid. Owing to the decreased amount of blood in the skin in chloroform anæsthesia it is sometimes difficult to observe the onset of cyanosis, and it is often considered advantageous to use oxygen in conjunction with the Junker bottle, the gas being passed through the chloroform.

Chloroform is also administered as an analgesic in obstetrics in friable glass capsules containing 20 to 60 minims (*v. infra*).

[P1] **Chloroform Mixtures.**

A.C.E. (dehydrated alcohol 1, chloroform 2, ether 3) and C.E. (chloroform 2, ether 3) were formerly much used in the belief that they were safer than either chloroform or ether used separately.

The ether stimulates the respiration and also the circulation, thus counteracting the effects of the chloroform. For abdominal operations, the addition of chloroform to ether ensures the requisite shallow breathing being obtained without the profound depth of anaesthesia necessary with ether alone, provided pre-anaesthetic sedatives have not been given. The disadvantage of the mixtures is that owing to the difference in the rates of evaporation of the constituents the composition of the vapour inhaled by the patient is quite different from that of the liquid mixture. With C.E. mixture the patient inhales alternately almost pure ether and almost pure chloroform. Approximate uniformity in composition may be obtained by using some form of Shipway's apparatus in which the air or oxygen is passed through separate bottles of the constituent anaesthetic agents arranged in parallel, but mixtures are now rarely used.

#### Chloroform Analgesia in Labour.

Capsules containing 20, 30, and 60 minims and encased in cotton wool and silk are made for use by midwives during labour.

Of all the drugs used for the assuaging of the pains of labour, chloroform is the most satisfactory under the prevalent conditions of ordinary domiciliary midwifery, but a limit must be set on the quantity used, and the degree of anaesthesia must be shallow.—F. Roques, *Lancet*, i/1933, 179.

An investigation on 100 cases at the Queen Mary's Maternity Home, Hampstead, showed that in 84% of cases there was no apparent effect on uterine contractions, while 16% showed a decrease. In 95% there was apparent lessening of pain; voluntary effort was affected in 60%, diminished in 37%, and increased in 3%. 92% of patients expressed themselves in favour of the capsules. In no case was there any ill effect on the child. Nine of the cases became excited under the chloroform, in 6 cases there was delay in the second stage, and in 8 cases loss above normal during the third stage. It would seem established that the use of chloroform capsules by midwives in the second stage of labour is both safe (but not when the midwife is conducting the case alone) and in the majority of cases beneficial to the patient. The average number of capsules used was 3.41 and the average interval between each capsule 10.16 minutes.—Arthur Rees, *Brit. med. J.*, ii/1933, 241.

The capsules have been an enormous boon in the obstetric departments of L.C.C. hospitals.—E. W. Masterman, *Brit. med. J.*, i/1933, 347. No bad effects in 861 cases, save that 5% of patients became noisy. Labour was not prolonged.—Letitia Fairfield, *ibid.*

Chloroform by any method should not be used by midwives acting alone. This conclusion has been reached with regret, but both the immediate and delayed dangers which are well recognised occurred in this investigation, and it is not possible fully to guard against such occurrences if the administration of chloroform is in inexperienced hands.—Report on Investigation by the College of Obstetricians and Gynaecologists at the request of the National Birthday Trust Fund, per *Lancet*, i/1936, 283.

### GENERAL PREPARATIONS OF CHLOROFORM

**Aqua Chloroformi (B.P.).** 1 in 400 of water. *Fr. Cx.*, *F.E. VIII* and *P. Ital. V*, 1 by weight in 200. *U.S.P. XI* has a saturated solution.

*Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.).

Salts, e.g., sodium sulphate, are apt to cause deposition of chloroform from aqueous solution.

**Aqua Chloroformi Concentrata (B.P.C.).** *Dose.*—6 to 12 minims (0.4 to 0.8 ml.). 1 in 10.

**Aqua Chloroformi Duplex (B.P.C.).** *Syn.* AQUA CHLOROFORMI FORTIOR. *Dose.*—2 to 4 drachms (8 to 16 ml.). 1 in 200.

[P1] **Chloroformum Camphoratum (B.P.C.).** Camphor 2 (by weight) dissolved in chloroform 1 (by volume).

Useful for toothache, applied on cotton wool.

[P1] **Chloroformum Mastiche.**

Mastiche 1, chloroform *q.s.* to 2.

**Emulsio Chloroformi (B.P.C.).** *Dose.*—5 to 30 minims (0.3 to 2 ml.).

Chloroform, 1 in 20, with tincture of quillaia, mucilage of tragacanth and water. It is of the same strength as Spiritus Chloroformi.

[P1] **Guttæ Chloroformi cum Menthol Compositæ.**—SELF-INFLATOR DROPS. Menthol 15 gr., chloroform  $\frac{1}{2}$  oz., acetic ether and alcohol 90% of each 2 dr.

*Directions.*—2 or 3 drops to be placed upon the wool in the inflator on each occasion of use.

**CHRONIC TYMPANIC AND EUSTACHIAN CATARRH.** Value depends to an extent on the ease with which air containing a little chloroform passes up the Eustachian tubes. Inflation with a Eustachian Self-Inflator is conducted as follows:—Drop the amount prescribed on the wool in the mouth-piece with a dropper. With the mouth-piece held firmly between or against the lips (according to the form of the instrument) and the nose-piece tightly in the freer of the two nostrils, compress the other nostril to close it completely. Draw a breath (not through the instrument) and then blow through the mouthpiece so as to puff out the cheeks and “crack the ears.” If vapour is too irritating blow through the instrument a few times before use. To concentrate the effect on the right ear, close firmly with the finger the left ear and bend head sideways over the left shoulder—*vice versa* for the left ear.

The duration of treatment should be controlled by the prescriber.

For the Medicated Politzer Apparatus in which these drops may be used, see Dundas Grant, *Practitioner*, June, 1925.

[P1] **Linimentum Chloroformi (B.P.C.).**

Chloroform 1, liniment of camphor 1.

[P1] **Linimentum Chloroformi (U.S.P. XI).**

Contains at 25° from 35 to 45% *w/v* of chloroform, and is made by agitating together 3 volumes of chloroform with 7 volumes of camphor and soap liniment.

[P1] **Mist. Tuss. Nig. (N.I.F.).**

Tincture of chloroform and morphine 10 m., liquid extract of liquorice 10 m., water to  $\frac{1}{2}$  oz.

**Oleum Chloroformii (P. Jap. V).** Chloroform and olive oil, equal parts.

**Spiritus Chloroformi (B.P.).** *Syn.* CHLORIC ETHER. 1 in 20 of alcohol 90%.

*Dose.*—5 to 30 minims (0.3 to 2 ml.).

**Spiritus Chloroformi (U.S.P. XI).**

*Average dose.*—30 minims (2 ml.).

Chloroform 8.5 to 9.25% *w/v*, in alcohol. 6% by volume.

[P1] **Tinctura Chloroformi Composita (B.P.C.).** *Dose.*— $\frac{1}{2}$  to 1 drachm (1 to 4 ml.). Chloroform 10% *v/v* with alcohol 90% and compound tincture of cardamom.

[P1-S1] **Tinctura Chloroformi et Morphinae (B.P.C.).**

*Syn.* CHLORODYNE, TINCT. CHLOROF. ET MORPH. (B.P. '85).

*Dose.*—5 to 10 minims (0.3 to 0.6 ml.).

10 minim dose contains chloroform  $1\frac{1}{2}$  m., ether  $\frac{1}{2}$  m., alcohol 90%  $1\frac{1}{2}$  m., morphine hydrochloride  $\frac{1}{8}$  gr. (equivalent to 0.18% of anhydrous morphine), and dilute hydrocyanic acid  $\frac{1}{2}$  m., with oil of peppermint, liquid extract of liquorice, treacle and syrup *q.s.*

Poisoning by 4 ounces of chlorodyne, with recovery by use of atropine, strychnine, and stimulants is recorded.

[D-P1-S1] **Tinctura Chloroformi et Morphinae Composita (B.P.C.).**

*Dose.*—5 to 15 minims (0.3 to 1 ml.).

Contains 7.5% *v/v* of chloroform, 1% *w/v* of morphine hydrochloride and 10% *w/v* of tincture of cannabis.

10 minim dose contains: chloroform  $\frac{3}{4}$  m., morphine hydrochloride  $\frac{1}{4}$  gr., dilute hydrocyanic acid  $\frac{1}{2}$  m., tincture of capsicum  $\frac{1}{4}$  m., tincture of Indian hemp 1 m.

Contains approximately four times the proportion of morphine present in *Tinctura Chloroformi et Morphineæ*.

[D.P.1-81] **Chlor-Anodyne** (*Parke, Davis, London*). Containing in each fluid ounce, morphine hydrochloride  $2\frac{1}{2}$  gr., chloroform 46 m., fluid extract of cannabis indica 46 m., dilute hydrocyanic acid 9 m., etc. For use in colic, acute gastro-enteritis, etc. *Dose*.—5 to 15 minims.

## ANÆSTHETIC HYDROCARBONS

**Ethyleneum** (*B.P., U.S.P. XI*). *Syn.* OLEFIANT GAS.  
 $\text{CH}_2 : \text{CH}_2 = 28.03$ .

The first member of the olefine series of hydrocarbons—*i.e.*, the series in which a double linkage occurs. Ethylene is a colourless gas with slight ethereal odour. It has sp. gr. 0.9784 (air = 1). It burns in air with a bright flame and forms an explosive mixture with 3 vols. of oxygen. At 0° and under a pressure of 42.5 atmospheres it is converted into a colourless liquid which boils at -102°. It is a constituent of illuminating gas.

**Soluble** in 9.2 vols. of water, in 0.5 vol. of alcohol 95% and in about 0.05 vol. of ether, at 25°.

**Uses.** Ethylene is used as an anæsthetic, particularly in America. It is administered with 10 to 20% of oxygen in a manner similar to that of nitrous oxide. It is a more potent narcotic than nitrous oxide, hence more oxygen can be given and greater muscular relaxation obtained without dyspnœa. Recovery is rapid, consciousness returning in from one to five minutes, and vomiting occurs less frequently than after ether or chloroform. The smell is disagreeable but the senses are soon dulled. It is inflammable, and mixtures with air or oxygen are explosive. Muscular relaxation is less complete than that obtained with ether, but it has no irritant action on the respiratory tract.

A survey of 425,000 ethylene anæsthesias shows it is probably as safe as ether, if not safer. The quantity of ethylene capable of explosion is too small to produce considerable damage.—*M. Salzer, J. Amer. med. Ass.*, i/1929, 2097.

Much more satisfactory than nitrous oxide—could be used with as much as 20 to 30% of oxygen. Dangerous with cautery or diathermy.—*I. W. Magill, Lancet*, i/1931, 353.

For dental work its smell and risk of fire is a disadvantage.—*R. R. Macintosh, Brit. Dental J.*, Feb. 15, 1932.

Used with excellent results in a series of 525 operations on children, but use discontinued owing to the "appalling" headaches from which both anæsthetist and surgeon suffered afterwards.—*R. Jarman, Brit. med. J.*, ii/1932, 883.

In answer to a questionnaire, no fewer than 757,815 administrations alone, and 267,560 in combination with ether, are recorded.—*J. Amer. med. Ass.*, ii/1933, 1716. For earlier references see 21st Edition, Vol. I.

**Acetylenum.**  $\text{CH} : \text{CH} = 26.02$ . The initial member of the acetylene series of hydrocarbons (*i.e.*, with triple linkage); a gas with unpleasant odour. It has sp. gr. 0.92 (air = 1), and is compressible into a liquid which has explosive properties. It is more soluble than ethylene in alcohol.

Acetylene is a general anæsthetic with action similar to that of ethylene. Following clinical investigations by Gauss in 1923 it had a certain vogue in



America, especially among gynecologists, but it has been little used in this country. The disagreeable odour and the explosive risk have probably militated against its wider use. For anæsthetic use it is employed as a mixture consisting of acetylene 40% and oxygen 60% with the addition of oil of pine to mask the smell.

### Cyclopropanum (U.S.P. XI Supp. II).

*Syn.* TRIMETHYLENE.  $\text{CH}_2 \cdot \text{CH}_2 \cdot \text{CH}_2 = 42.05$ .

Cyclopropane, an isomer of propylene ( $\text{CH}_3 \cdot \text{CH} : \text{CH}_2$ ), is a colourless gas prepared by the action of zinc on 1 : 3-dibromopropane. It is heavier than air, with a density of 1.46, and is inflammable and explosive in concentrations of from 20 to 75% when mixed with oxygen. Cyclopropane has a characteristic sweetish odour not unlike chloroform or ethylene. B.p.—34.5°.

**Soluble** in 2.7 vols. of water at 15°; freely soluble in alcohol, ether, chloroform and oils.

**Uses.** Cyclopropane is an anæsthetic effective in low concentration, profound anæsthesia being produced by a concentration of 18%. Muscular relaxation is better than with nitrous oxide, but not as complete as with ether. It is not irritant to the respiratory tract and induction is pleasant, smooth and rapid. Recovery is rapid, nausea and vomiting are less frequent than with ether, and there are fewer post-operative complications.

The chief disadvantages connected with its use are the explosibility of anæsthetic mixtures of cyclopropane and oxygen, the increased hæmorrhage from the raised blood pressure, and the tendency to respiratory depression. On the other hand, the extremely high percentage of oxygen compatible with full anæsthesia, and the absence of irritation to the respiratory passages, render it particularly suitable for major thoracic surgery and bad risk cardiac cases.

As regards after-effects, Schmidt and Waters, in America, investigated 2200 cases anæsthetised with cyclopropane-oxygen, and compared them with 2200 similar operations performed under nitrous oxide and oxygen and ethylene-oxygen, the closed-circuit technique being used in each case. The figures for vomiting and respiratory complications were in favour of cyclopropane, but there were more circulatory complications and post-operative deaths than with the older methods.—C. L. Hewer, *Proc. R. Soc. Med.*, Jan., 1936, 262.

Induction is always pleasant for the patient, with no sensations of bursting, throbbing or choking, such as are sometimes complained of with other anæsthetics. Although the odour of cyclopropane as it issues from the cylinder is not pleasant, patients are not aware of it during induction, nor do they complain of unpleasant taste or smell during the recovery period such as occurs with ether. Complete abdominal relaxation always obtained although it has often been necessary to increase respiratory exchange by artificial methods. When this is resorted to it must be borne in mind that one is dealing with an extremely potent agent which is not without its effect on the heart muscle. The fact that cyclopropane is neither a respiratory stimulant nor an irritant makes it necessary that the anæsthetist should exercise the greatest care in its administration; but in the hands of the expert it is to be considered an anæsthetic of great utility and value.—S. Rowbotham, *Proc. R. Soc. Med.*, Jan., 1936, 260.

It can be satisfactorily administered by the endotracheal method. It is applicable to extremes of youth and age and has advantages over ether in operations on very small babies. Cyclopropane most nearly approaches the ideal anæsthetic.—H. R. Griffith, *Canad. med. Ass. J.*, i/1937, 496.

In a study of 1333 administrations of cyclopropane the outstanding observation was the relatively low figure both for the incidence of pulmonary morbidity and

for the morbidity-mortality ratio.—G. E. Burford, *J. Amer. med. Ass.*, i/1938, 1087.

Post-operative pulmonary complications are much less frequent than with other anaesthetics; nausea and vomiting are less frequent than with ether, but more frequent than with nitrous oxide alone. Recovery is rapid, being almost instantaneous after a short administration and from five to ten minutes after a long administration.—L. B. Mevill, *Edinb. med. J.*, 1939 (*Trans. Medico-Chir. Soc. Edinb.*, 70).

A combination of spinal anaesthesia (Percaine, 1 in 2000) with cyclopropane general anaesthesia was used in 70 major operations, mostly abdominal. The combination forms a pleasant and effective anaesthetic for the patient, and is a material aid to the surgeon, in operations on the upper abdomen.—H. Dodd and J. T. Hunter, *Lancet*, i/1939, 685.

**Explosion hazard.** As the result of a questionnaire sent to 100 anaesthetists it was found that among two and a third million administrations the explosion rates of ether, ethylene and cyclopropane were all very low, and all fell in the neighbourhood of from 2 to 4 per 100,000 anaesthetics. The mortality rates were too low to be figured since there were only two deaths among the 2½ million cases.—P. D. Woodbridge, *J. Amer. med. Ass.*, ii/1939, 2308.

**Vinyl Ether.** *Syn. and Prop. Name.* VINETHENE, VINESTHENE (Merck, New York; *Pharmaceutical Specialities* (May & Baker) Ltd., London).  $(CH_2 : CH)_2O = 70.05$ .

A volatile, clear, practically colourless liquid with a characteristic odour.

B.p.  $28^\circ$  to  $31^\circ$ ; sp. gr. 0.77. Readily decomposed in air and light into formaldehyde and formic acid, and polymerises to a jelly. Supplied containing 0.01% of phenyl- $\alpha$ -naphthylamine as an antioxidant and also 3.5% of dehydrated alcohol to prevent breath freezing owing to rapid evaporation when used as an anaesthetic.

**Uses.** Vinyl ether is used as an inhalation anaesthetic for short anaesthetics. It is more potent than ether, with more rapid induction and recovery. Post-operative complications are rare and nausea and vomiting less frequent than with chloroform. It is usually employed by the "open drop" method (60 to 80 drops per minute), but its use by this method should not exceed thirty minutes. It has found considerable use in dental practice and in obstetrics.

The anaesthetic potency is 4 times that of ether and greater than that of chloroform as 1:3 is to 1, and there is a wider "margin of safety" than with ether or chloroform. A few inhalations are sufficient to produce anaesthesia, there is very little excitement, any desired degree of muscular relaxation can be obtained, and recovery is very rapid. Respiration is not interfered with as much as with ether, and tests for liver function show practically no liver change. Results from its use in 50 and 102 obstetrical cases show it to be a very suitable anaesthetic for employment in obstetrics, with minimal danger to mother and child.—Wesley Bourne, *Lancet*, i/1934, 566.

Vinyl ether seems to be particularly suitable for obstetric anaesthesia in general practice on account of its safety for mother and child, its ease of administration, the rapidity of its action, the satisfactory maintenance of any desired degree of narcosis, and the early uneventful recovery. Although vinyl ether may be given with relative safety by the "open drop" method, it is preferable to administer it in a "closed" manner with oxygen.—Wesley Bourne, *J. Amer. med. Ass.*, ii/1935, 2047.

It is not recommended that the drug be used for periods exceeding 30 minutes, and those employing it for any period should familiarise themselves with the nature of the compound. Rapid induction is an advantage, provided over-concentration and excessive anaesthesia are avoided, and rapid recovery is also an advantage.—Rept. of Council on Pharmacy and Therapy A.M.A., *J. Amer. med. Ass.*, ii/1937, 656.

Employed as a general anæsthetic in a series of 100 infants and children ranging from one month to 11 years of age. It was found extremely satisfactory when given by the open mask method for minor operative procedures of 5 or 10 minutes' duration, and in no case was there any alarming or untoward reaction accompanying or following the anæsthesia.—R. E. Gross, *New Engl. J. Med.*, i/1939, 334.

In Vinesthene and Vinesthene mixture we have an anæsthetic of the greatest value to the general practitioner and well within his means. The use of the drug will facilitate the production and maintenance of anæsthesia and assist both practitioners and patient.—J. Elam, *Lancet*, ii/1939, 1115.

Vinesthene is becoming increasingly popular as an anæsthetic for the trivial operations of general practice. Although it has been found unreliable for producing the deep muscular relaxation often required for abdominal surgery, it has a sphere of usefulness in extra-abdominal surgery which may be of particular value in war casualties. Its advantages include portability, quick induction and recovery and comparative freedom from after-effects.—R. R. Macintosh and F. B. Pratt, *Brit. med. J.*, ii/1939, 1079.

A series of 200 children were given anæsthesia for extraction of teeth with (a) vinyl ether or (b) ethyl chloride. The results showed that these are both safe and useful anæsthetics. The action of vinyl ether is shorter and less certain than that of ethyl chloride, but it is useful for producing a short anæsthesia for the extraction of a few deciduous teeth in young children. Vinyl ether is more likely to cause struggling during the induction period and causes troublesome salivation in many cases. Recovery is much more rapid than from ethyl chloride and is less likely to be accompanied by vomiting.—J. O. French *et al.*, *Brit. med. J.*, i/1940, 432.

**Convulsions.** During a series of 2406 Vinesthene anæsthesias there have been nine cases of convulsions, none of them fatal. The cause of the convulsions is obscure, but it is recommended that anæsthesia with Vinesthene should not exceed an hour in duration.—C. J. M. Dawkins, *Brit. med. J.*, i/1940, 163.

## CHROMII TRIOXIDUM

*B.P., U.S.P. XI, P. Helv. V, P.G. VI, P. Dan.*

$\text{CrO}_3 = 100.0$ .

*Syn.* ACIDUM CHROMICUM, CHROMIC ANHYDRIDE (*Fr. Cx.*).

In deliquescent, crimson crystals. A powerful oxidising agent.

**Caution:** Incompatible with alcohol, glycerin and other oxidisable substances. **Soluble** about 5 in 3 of water.

**Gargarisma Chromii Trioxidi (B.P.C.).** 0.2% *w/v*.

**Liquor Chromii Trioxidi (B.P.C.).** *Syn.* LIQUOR ACIDI CHROMICI.

25% *w/v* in water. *Fr. Cx.* has 50% *w/v*.

**Uses.** Caustic, astringent and germicidal. Applied to warts, to condylomata and lupus; 1 in 40 to ulcerated gums and mouth sores. For sweating feet 5 to 10% lotion; in leucorrhœa and ozæna 1 in 2000. In secondary syphilis of the pharynx, the so-called snail-track ulcer treated with a solution (10 grains to the ounce). For mucous and warty patches 5% is useful. A 10% solution brushed on daily with alternately boric acid and zinc ointment has been employed in the treatment of rodent ulcer.

In ulcerative stomatitis chromium trioxide used warm 1 in 200 to 1 in 400 and applied with wool round a probe relieves pain and removes the necrotic tissue. Immediately after the use of the chromic lotion paint the affected area with a mixture of 20 gr. of chlorbutol to the ounce of equal parts glycerin and spirit.

**CHROMIUM PLATING.** The process consists in wiring the articles to a frame ready for the plating vat, the actual plating (anything up to 15 mins.), unwiring, swilling and polishing. Current 500 to 1000 amps. and 4 to 10 volts. Solution contains 50% of chromic acid. Fumes contain the acid forced up in spray by the evolution of hydrogen at the cathode. Lassar's paste modified with a preponderant base of soft paraffin smeared on hands and arms before work, and a little instilled into each nostril. Soap containing free lanolin used in some works. Dermatitis treatment—double strength calamine solution. When oedema subsides scrub spots with gauze soaked in spirit, dry, and wrap in lint and Lassar's paste. Chromium ulcers should be cleaned and dressed with zinc oxide and soft paraffin. Ulceration of the nose treated with gauze soaked in flavine 1 in 1000.—H. B. Trumper, *Brit. med. J.*, i/1931, 705.

The use of chromium and its salts is steadily increasing industrially. The industries concerned are (1) electrolytic chromium plating, (2) the manufacture of colours containing chromium, e.g., lead chromate, (3) chromium tanning of skins, which is replacing vegetable tanning, (4) dyeing fabrics and furs, (5) dyeing certain woods, (6) the manufacture of sporting powders, (7) photography, (8) the manufacture of Swedish matches. Contact with the salts of chromium causes first erythema and then eczema; if the skin is anywhere abraded, a chemical reaction with the underlying tissue occurs, setting up tissue necrosis with the formation of painful, indolent ulcers, and in the presence of dust or fumes the mucous membrane of the nasal cavity is attacked. Symptoms of general poisoning are not usual, but anæmia occurs amongst those preparing chromates.—Leroux-Robert, *Bull. Acad. Méd., Paris*, 1936, 116, 875.

**Potassii Chromas.**  $K_2CrO_4 = 194.2$ . In yellow crystals soluble in water. Used as a reagent.

**Potassii Dichromas (B.P.C.).** *Syn.* POTASSIUM BICHROMATE (*Fr. Cx.*).  $K_2Cr_2O_7 = 294.2$ .

*Dose.*— $\frac{1}{10}$  to  $\frac{1}{2}$  grain (0.006 to 0.012 g.).

An odourless, orange-red, crystalline substance with an acid taste.

**Soluble** 1 in 10 of water; insoluble in alcohol.

**Antidotes.** Empty stomach by emetic or stomach tube. Give magnesia or chalk freely in water. Demulcent drinks. Keep patient lying down and warm; give stimulants if necessary.

Dermatitis may follow the contact of potassium dichromate with the skin of susceptible persons. This may be avoided by frequently rinsing the exposed skin with a saturated solution of sodium bisulphite and then water.

**Uses.** In dyspepsia and gastric ulcer, in capsules or as pills massed with kaolin ointment. It has also been used, in the form of a 5% solution for external application, in the treatment of hyperhidrosis of the feet, and a 10% solution has been employed as a caustic to warts and nasal polypi.

## CHRYSAROBINUM

*B.P., U.S.P. XI, P. Jap., P. Ned. V, P. Helv. V, P. Dan., P. Ital. V, F.E. VIII.*

*Syn.* Commonly but erroneously called CHRYSOPHANIC ACID; ARAROA DEPURATA (*P. Austr.*).

*Dose.*— $\frac{1}{4}$  to  $\frac{1}{2}$  grain (0.01 to 0.03 g.).

A yellow, tasteless microcrystalline powder obtained from araroba by extraction with hot benzene. Is a mixture of chrysophanol-anthranol,  $C_{15}H_{12}O_3$ , and related substances.

**Soluble** slightly in alcohol 90%, 1 in 16 of ether, 1 in 12 of chloroform, 1 in 18 of benzene, also in fats; almost insoluble in water.

**Uses.** Has been employed internally in psoriasis, but is extremely irritant and may give rise to diarrhoea, vomiting and hæmaturia. Externally as ointment or pigment. Chrysarobin is a powerful stimulant and parasiticide in acne rosacea, alopecia, psoriasis, lupus, ringworm of the scalp, pityriasis and tinea circinata.

[P1] **Pigmentum Chrysarobini (B.P.C.).**

Chrysarobin 10% *w/v* in solution of gutta-percha.

In psoriasis, painted on twice a day with a brush for ten days without washing—finally washing off.

**Pigmentum Chrysarobini et Pyrogallolis.**

Chrysarobin 1, pyrogallol 1, ether and alcohol, of each 10, collodion 120. Apply after bathing, every third day for psoriasis and ringworm.

[P1] **Suppositorium Chrysarobini.**

Chrysarobin 1½ gr., iodoform, ½ gr., belladonna extract ½ gr., glycerin *q.s.* to make a suitable paste and oil of theobroma *q.s.* to 30 gr. Gives good results in hæmorrhoids.

**Unguentum Chrysarobini (B.P.).**

4% in simple ointment.

It stains the skin and hair, and a strong ointment after three days' continued use sometimes produces feverishness and irritation. 5 to 10 gr. to 1 oz. may be better. The ointment should not be employed over a large area of skin. Its stains can be removed by benzene, weak solution of potash or chlorinated lime. Will effect a cure of tinea cruris in six days if applied thickly on lint twice daily.

**Unguentum Chrysarobini (U.S.P. XI).**

Chrysarobin 6, wool fat 5, yellow wax 5, chloroform 4, liquid paraffin 6, yellow soft paraffin to 100.

**Unguentum Chrysarobini Compositum (B.P.C.).**

Chrysarobin 4, ichthammol 4, salicylic acid 2, in yellow soft paraffin to 100.

**Unguentum Chrysarobini Compositum (St. J. H.).**

Chrysarobin 25 gr., ichthammol 25 m., salicylic acid 10 gr., soft paraffin to 1 oz. Psoriasis is treated by an ointment of chrysarobin 5, salicylic acid 2½, oil of birch tar 5, soft soap 6½, soft paraffin 6½.

Controlled clinical experiments show that an ointment of chrysarobin and soft paraffin is not superior to chrysarobin paste, but its irritant effect is three times greater. The addition of salicylic acid only slightly improves the curative effect of chrysarobin paste but it intensifies the irritant effect of the chrysarobin. The addition of liquid soap to chrysarobin paste renders the preparation non-irritant but entirely inefficient.—H. W. Siemens, per *Brit. med. J. Ept.*, i/1938, 60.

**Chrysarobin Tri-Acetate.** A brownish powder recommended as a substitute for chrysarobin. Solutions of 2 to 3% are said to be effective and free from toxic effects; non-irritant, and do not stain. It is soluble in ether, chloroform and in acetone.

**Araroba (B.P.C.). Syn. GOA POWDER, CRUDE CHRY SAROBIN.**

A brownish concretion from the cavities in the trunk of *Andira Araroba* (Leguminosæ), dried and powdered.

Crude araroba is imported from Brazil; it contains about 50% of chrysarobin. The Indian mode of using the drug is to cut a lime fruit, dip it in the powder

and dab it on the affected skin. The Brazilians mix it with vinegar. Has been used as an ointment (1 in 16 to 1 in 32 with lard) as a parasiticide.

**Dithranol.** *Syn. and Prop. Names.* DIHYDROXYANTHRANOL, ANTHRAROBIN (*P. Dan.*), ANTHRALIN (*Abbott Laboratories, London*), CIGNOLIN (*Bayer Products, London*), DEROBIN (*Glaxo Laboratories, London*).  $C_{14}H_{10}O_3 = 226.08$ .

1 : 8-Dihydroxyanthranol, occurring as a yellowish, crystalline powder, m.p.  $176^{\circ}$ .

**Insoluble** in water but soluble in organic solvents, oils, oleic acid and in dilute sodium hydroxide, the latter solution having a green fluorescence.

**Stains** caused by dihydroxyanthranol may be removed from clothing with petrol, and from the skin with olive oil.

**Uses.** Dihydroxyanthranol possesses properties similar to those of chrysarobin, but is three or four times as active therapeutically. It is less toxic than chrysarobin and less likely to cause dermatitis, but the reaction of the patient should be tested by applying a 0.25% ointment before application to the head or face. It is indicated in the treatment of psoriasis, chronic eczema, alopecia areata, and dermatophytosis, applied in the form of an ointment varying in strength from 0.25 to 3% twice a day.

## CINCHONA

### B.P.

**Dose.**—5 to 15 grains (0.3 to 1 g.).

Consists of the dried bark of cultivated trees of *C. Calisaya*, *C. Ledgeriana*, *C. officinalis* and *C. succirubra* (Rubiaceæ), and of hybrids of either of the last two with either of the first two. It contains not less than 6% of total alkaloids of which not less than one-half consists of quinine and cinchonidine. CORTEX CHINCHON (*P. Helv. V, P.G. VI*) is from *C. succirubra*. CINCHONA (*U.S.P. XI*) is from *C. succirubra*, *C. Ledgeriana*, *C. Calisaya* and hybrids. *P. Ital. V* prescribes *Calisaya* or *succirubra* bark. *F.E. VIII* has *Calisaya*, *Loja* and *succirubra*. *P. Belg. IV* has *C. succirubra* and "other species", and *Fr. Cx.* includes *C. Calisaya*, *Quinquina Jaune*, *C. officinalis*, *Quinquina Gris*, and *C. succirubra*, *Quinquina Rouge*.

The principal dried barks used for the production of the salts of the cinchona alkaloids are:—Red cinchona bark, from *Cinchona succirubra*, containing 6 to 9% of total alkaloids, 1.5 to 3.5% being quinine; yellow cinchona bark, obtained from *C. Calisaya*, containing 6 to 7% of alkaloids, 3 to 4% being quinine; pale cinchona bark (crown or Loxa bark), from *C. officinalis*, containing about 6% of alkaloids of which half may be quinine; ledger bark, from *C. Ledgeriana*, which may contain up to 10 to 14% of quinine.

The quinine barks, as they are called, now imported from South America, are chiefly the *Calisaya* in quills. A large quantity of

bark, the produce of *C. succirubra*, *C. officinalis*, and hybrids, is grown in Madras and other parts of India.

Nine-tenths of the world's supply of bark consists of the rich Java bark, produced by *C. Calisaya* var. *Ledgeriana*.

For further references to the cultivation of cinchona, see 21st Edn., Vol. II, p. 117.

**Uses.** The bark in the form of the liquid extract, tincture and its alkaloids has extended use as a bitter tonic. Taken, as such, in powder form it is astringent, giving a feeling of warmth in the epigastrium and occasionally causing vomiting. For further data see the alkaloids quinine, quinidine, etc.

**Decoctum Cinchonæ Concentratum (B.P.C.).** Dose.—1 to 2 drachms (4 to 8 ml.). When Decoctum Cinchonæ is prescribed this concentrated decoction diluted with seven times its volume of distilled water may be dispensed.

**Elixir Cinchonæ (B.P.C.).** Dose.— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Tincture of cinchona, 1 in 6 $\frac{1}{2}$ , in syrup, glycerin and aromatic elixir.

**Elixir Calisayæ** is the same prepared with tincture of *Cinchona Calisaya*.

**Extractum Cinchonæ (B.P.).**

Dose.—2 to 8 grains (0.12 to 0.5 g.). Contains 10% w/w of cinchona alkaloids. A concentrated standardised extract from which the liquid extract, tincture and other preparations may be obtained by dilution.

**Extractum Cinchonæ Flavæ (Fr. Cx.)** is a dry extract prepared with 60% alcohol from *C. Calisaya* and containing 12% of total alkaloids.

**Extractum Cinchonæ Rubræ (Fr. Cx.)** is a soft aqueous extract made from *C. succirubra* and containing 8% of total alkaloids.

**Extractum Cinchonæ Liquidum (B.P.).**

Dose.—5 to 15 minims (0.3 to 1 ml.).

Contains 50% w/v of extract of cinchona, equivalent to 5% w/v of total alkaloids, with hydrochloric acid, glycerin, alcohol and water.

If prescribed with acid, as in the following:—Spirit of chloroform 1 $\frac{1}{2}$  dr., nitrohydrochloric acid 1 $\frac{1}{2}$  dr., liquid extract of cinchona 1 $\frac{1}{2}$  dr., water to 6 oz., mix the first three in order as written, and pour into the water to produce best result.

**Extrait de Quinquina Rouge (Fluide) (Fr. Cx.)** is made by percolation with dilute hydrochloric acid and contains 3.5% of total alkaloids. *P. Ital. V* contains 5% of total alkaloids.

**Infusum Cinchonæ Acidum Concentratum (B.P.C.).**

Dose.— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.). 1 in 2 $\frac{1}{2}$ .

**Infusum Cinchonæ Recens (B.P.C.).**

Dose.— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.). 1 in 20, with 1 in 80 of aromatic sulphuric acid.

**Mist. Cinchon. Acid. (N.I.F.).**

Liquid extract of cinchona 10 m., dilute phosphoric acid 10 m., glycerin 10 m., water to  $\frac{1}{2}$  oz.

**Mist. Cinchon. Ammon. (N.I.F.).**

Liquid extract of cinchona 10 m., ammonium carbonate 3 gr., chloroform water to  $\frac{1}{2}$  oz.

**Tinctura Cinchonæ (B.P.).** Dose.— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Extract of cinchona 10% w/v, in alcohol 70%.

**Tinctura Cinchonæ Composita (B.P.).** *Syn.* HUXHAM'S TINCTURE OF BARK. Dose.— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Extract of cinchona, 5% *w/v*, with orange peel, serpentry and cochineal.

**Tinctura Cinchonæ Composita (U.S.P. XI).**

*Average dose.*—60 minims (4 ml.).

Cinchona 10, bitter orange peel 8, serpentaria 2, in alcohol, with glycerin and hydrochloric acid but without cochineal.

**Tinctura Cinchonæ Rubræ (Fr. Cx.).** Red cinchona bark 1 in 5 with alcohol 60%.

**Vin de Quinquina Officinal (Fr. Cx.).**

*Dose.*— $\frac{1}{2}$  to 5 ounces (15 to 150 ml.).

Macerate cinchona 25 with dilute hydrochloric acid 2, alcohol (60%) 75, for 24 hours, shaking occasionally. Add red wine 920, macerate 24 hours and filter.

*Fr. Cx.* also includes Cinchona wine made from liquid extract of red cinchona 3, alcohol 60% 5, red wine 92 parts, all by weight.

**Vinum Chinæ (P. Jap. V).** Liquid extract of cinchona 5, sherry 80, sugar 14, tincture of orange 1.

**Vibrona (Fletcher, Fletcher & Co., London).** A wine containing the alkaloids of cinchona. A wineglassful contains the combined alkaloids of 5 gr. of cinchona bark in the form of hydrobromides. Total alkaloidal content 0.025%.

**Acidum Quinicum. Syn. KINIC ACID.**

$C_6H_7(OH)_2COOH \cdot H_2O = 210.1$ .

*Dose.*—4 to 8 grains (0.25 to 0.5 g.).

An acid contained in cinchona, principally combined with the alkaloids and with calcium, forms white crystalline masses, soluble in water about 5 in 6, and in alcohol 90% 1 in 35. It is decomposed into hippuric acid in the system. This and lithium quinate in similar dose have been used in gout and rheumatism.

**Alstonia (B.P.C.).**

The dried bark of *A. scholaris* (dita bark) from India and of *A. constricta* (Australian fever bark), from Australia (Apocynaceæ). Contains various alkaloids and is used in the East and in Australia in diarrhoea and in the treatment of malaria. **Infusum Alstoniæ.**

*Dose.*— $\frac{1}{2}$  to 1 oz. 1 in 20. **Tinctura Alstoniæ.** *Dose.*— $\frac{1}{2}$  to 1 drachm. 1 in 8.

**Cusparia (B.P.C.).** *Dose.*—10 to 30 grains (0.6 to 2 g.). *Syn.* ANGOSTURA BARK.

The bark of *Galipea officinalis* (Rutaceæ). Stimulant and tonic. In diarrhoea, dysentery and dyspepsia much employed in South America and West Indies. The bark is stated to contain cuspareine,  $C_{20}H_{19}NO_2$ , cuspareine,  $C_{18}H_{19}NO_2$ , and galipoidine,  $C_{18}H_{19}NO_2$ .

**Infusum Cuspariæ Concentratum (B.P.C.).**

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.). 1 in 2 $\frac{1}{2}$ .

When Infusum Cuspariæ is prescribed this concentrated infusion diluted with seven times its volume of water may be dispensed.

## CINCHOPHENUM

*B.P., P. Dan.*

$C_6H_5 \cdot C_9H_5N \cdot COOH = 249.1$ .

*Syn. and Prop. Names.* ACIDUM PHENYL CINCHONINICUM (P.G. VI, P. Helv. V, P. Ned. V, P. Svec. X, P. Ital. V, P. Belg. IV, F.E. VIII), ACIDUM PHENYLCHINOLINCARBONICUM, QUINOPHENUM (P. Jap. V), QUINOPHAN, 2-PHENYLQUINOLINE-4-CARBOXYLIC



ACID, AGOTAN (*Howard & Sons, Ilford*), ATOPHAN (*Schering, London*), PHENOQUIN (*Southall Bros. & Barclay, Birmingham*), TOPHOSAN (*Richter, London*).

[P1] "*Phenylcinchoninic acid; salicylcinchoninic acid; their salts; their esters.*"

[S1] "*Phenylcinchoninic acid; salicylcinchoninic acid; their salts; their esters.*"

[S4] "*Phenylcinchoninic acid; salicylcinchoninic acid; their salts; their esters.*"

**Dose.**—B.P. Add. I 5 to 10 grains (0.3 to 0.6 g.). B.P. '32 gave max. dose 15 grains. Is often given with sodium bicarbonate, as in the following scheme. 8 gr. thrice daily after meals. Simultaneously on the first day,  $\frac{1}{2}$  oz. (15 g.) and on the following days 75 gr. to 150 gr. (5 to 10 g.) of sodium bicarbonate in plenty of water.

A yellowish cream-coloured amorphous powder, melting at  $214^{\circ}$  to  $217^{\circ}$ .

**Soluble** 1 in about 120 of alcohol 95%, 1 in about 100 of ether and 1 in about 400 of chloroform. Insoluble in water. It dissolves in solutions of alkali hydroxides, bicarbonates and carbonates.

**Incompatible** with sodium bicarbonate and other alkalis *in vitro*.

**Toxic Effects.** Prolonged administration, especially to susceptible individuals, may give rise to skin rashes, palpitation, fall of blood pressure, cyanosis, vomiting, epigastric pain, hepatic dysfunction and jaundice. A careful watch should be kept for early signs of liver poisoning, *e.g.*, malaise and loss of appetite, and administration stopped at the first symptoms of intolerance.

Two cases terminating fatally following continued use (three  $7\frac{1}{2}$ -grain tablets daily).—L. J. A. Lowenthal, W. A. MacKay and E. Cronin Lowe, *Brit. med. J.*, i/1928, 592.

Forty-seven cases of cinchophen toxicosis published, with 10 deaths. Evidence of serious injury to liver in all cases.—H. S. Reichle, *J. Amer. med. Ass.*, ii/1929, 951.

Fatal case of poisoning. 45 grains a day for 4 days, with intermission for  $2\frac{1}{2}$  months. Death due to acute hepatitis.—W. Morris, *Brit. med. J.*, i/1931, 221. Should not be used as a routine measure in the treatment of gout. Details of 35 cases of jaundice following use.—T. G. Reah, *Lancet*, ii/1932, 504.

92 cases of poisoning have been recorded, 40 fatal—probably many cases of non-fatal toxicity are unrecognised and unreported.—H. A. Harris, *Brit. med. J.*, ii/1932, 707.

A fatal case of subacute yellow atrophy of the liver following taking of  $37\frac{1}{2}$  grains of cinchophen (Atophan) at the rate of one  $7\frac{1}{2}$ -grain tablet on 5 successive days.—T. N. Fraser, *Brit. med. J.*, ii/1934, 1195.

In the eight-year period from 1924 to 1932 inclusive, there were about 660,000 pounds of cinchophen produced and consumed, representing approximately 660 million doses of  $7\frac{1}{2}$  gr. each. Despite this, during this period there were only 38 reported deaths in the United States attributed to the use of this drug, making the chance toxic dose 1 : 17,000,000, which is as low as one could reasonably expect for any active therapeutic agent. Cinchophen is not a harmless drug, but it is a very effective one, and when used with proper care and reasonable precautions, its benefits far outweigh its limitations.—R. G. Snyder and co-workers, *J. Lab. Clin. Med.*, 1936, 21, 545.

**Antidotes.** (Chronic poisoning—from prolonged dosage.) Stop the drug. Keep patient in bed. Dextrose and fluids freely dextrose and insulin for severe cases.

**Uses.** Cinchophen possesses an analgesic and antipyretic action similar to that of the salicylates, and in addition causes an increase of uric acid excretion in the urine; this increase continues for 24 hours after administration of the drug, is followed by a compensatory decrease, and returns to normal in two to three days. Cinchophen is employed in the prevention and treatment of acute gout, in which it is stated to act more promptly than colchicum; it is also used with benefit in subacute and chronic gout, and is of value for the relief of pain in lumbago, sciatica and neuralgia. In order to minimise the possibility of liver damage, it is recommended that dextrose and calcium lactate should be given concurrently with cinchophen.

[P1-81-84] **Tabellæ Cinchopheni** (*B.P.C.*) contain 5 gr. (0.3 g.).

[P1-81-84] **Acitophosan** (*Richter, London*). A combination of calcium cinchophen and calcium aspirin. *Dose.*—3 to 6 8-grain tablets daily with plenty of fluids. Influenza, gout and rheumatic affections.

[P1-81-84] **Atophan Balsam** (*Schering, London*). Amyl ester of Atophan 10% w/w, phenyl salicylate, camphor and synthetic menthol in a neutral base. For external application in rheumatism, sciatica, gout, etc.

[P1-81-84] **Atophanyl** (*Schering, London*). Contains equal parts of sodium Atophan and sodium salicylate in solution.

*For intravenous injection.*—10 ml., containing 0.5 g. of each.

After injection, the arm should be held above the head for 1 to 2 minutes. Warm the ampoules first. The patient should not undertake undue exertion too soon after the pain has been relieved.

*For intramuscular injection.*—5 ml., containing 0.5 g. of sodium Atophan, 0.5 g. of sodium salicylate, and 0.3 g. of urethane in distilled water. To be given deeply in the upper external quadrant of the gluteal muscle.

In chronic cases, 10 to 15 injections are given; usually one injection per day for 4 days, followed by an interval of 2 to 3 days. Used for the same purposes as cinchophen.

[P1-81-84] **Gorun Cachets** (*T. Christy & Co., London*). A combination of cinchophen, hexamine, and glycocholl. Also in ampoules of solution for intramuscular injection. In sciatica, lumbago, etc.

[P1-81-84] **Hexophan** (*Bayer Products, London*). Oxyphenylquinoline-dicarboxylic acid. *Dose.*—1 or 2 7½-grain tablets thrice daily. In gout, rheumatism and lumbago.

[P1-81-84] **Neo-Phenoquin** (*Southall Bros. and Barclay, Birmingham*) is lithium phenylcinchoninate.  $C_6H_5C_6H_4N^+COOLi^- = 255.0$ .

*Dose.*—From 5 to 10 tablets daily, each tablet containing 0.25 g., after meals, followed by a glass of water. For elimination of uric acid in acute and chronic gout. Simultaneous use of sodium bicarbonate is sometimes desirable.

[P1-81-84] **Oxyl-Iodide** (*Lilly, London*). Phenylcinchoninic acid hydriodide, containing 33% iodine. In arthritis, neuritis and myositis.

[P1-81-84] **Sciatego** (*Coates & Cooper, London*). Dragées containing cinchophen, hexamine and glycocholl. *Dose.*—2 dragées twice daily for 2 or 3 weeks. Rheumatism, lumbago, sciatica.

[P1-81-84] **Tophamid** (*Richter, London*). Tablets contain 4 gr. each of phenylcinchoninic acid and amidopyrin. *Dose.*—1 or 2 tablets three times daily. Influenza and pyrexial conditions.

[P1-81-84] **Tophosanyl** (*Richter, London*). Sodium phenylcinchoninate 8 gr., sodium salicylate 8 gr., in ampoules of 10 ml. for intravenous injection.

[P1-81-84] **"Ung. Agotan Co."** (*Howard & Sons, Ilford*).

Agotan with a rubefacient in ointment form, for use in general, articular and muscular rheumatism, gout, lumbago, sciatica, erythema nodosum, torticollis, pleurodynia, neuritis, urticaria and chilblains. The simultaneous use of Agotan tablets *per os* increases results.

[P1-81-84] **Atoquinol** (*Ciba, Horsham*) is allyl phenylcinchoninate in tablets containing 4 gr. *Dose.*—4 to 8 tablets in 24 hours. They should be administered

with a large quantity of liquid, and if the urine shows a sediment of uric acid or urates, it is advisable to prescribe sodium bicarbonate as well.

It forms odourless yellowish crystals, m.p. 30°, insoluble in water, readily soluble in ether and oils. Has analgesic and antipyretic properties and is used similarly in arthritis, gout, neuralgia, sciatica, etc. It may be applied externally in an ointment (20%).

[P1-S1-S4] **Methyl Phenylcinchoninate** (*P. Ned. V Supp. II*). *Syn. and Prop. Name.* METHYL PHENYLCHINOLINCARBONATE (*P. Helv. V, P.G. VI*), METHYLCHINOPHENUM, NOVATOPHAN (*Schering, London*).  
 $C_{16}H_{15}N_2O_3$ ,  $\text{C}_6\text{H}_5\text{N}-\text{COOCH}_3$ , = 263.1.

*Dose.*—8 grains (0.5 g.) 4 times daily to 15 grains (1 g.) thrice daily. Simultaneously on first day  $\frac{1}{2}$  ounce (15 g.), and on the following day 75 to 150 grains (5 to 10 g.) of sodium bicarbonate.

This compound is the methyl ester of cinchophen and is used similarly. It occurs as yellowish tasteless crystals insoluble in water.

[P1-S1-S4] **Arcanol** (*Schering, London*). Tablets containing methylphenylcinchoninate  $7\frac{1}{2}$  gr. and acetylsalicylic acid  $7\frac{1}{2}$  gr. In influenza, etc.

**Neocinchophenum** (*B.P.C., U.S.P. XI*). *Syn. and Prop. Name.* ETHYL METHYLPHENYLCHINONINATE, TOLYSIN (*Calco Chemical Co., Bound Brook, N.J.; Martindale, London*).

*Dose.*—10 to 15 grains (0.6 to 1 g.) 3 or 4 times daily for 4 or 5 days. It may be necessary to give 100 grains daily in rheumatic fever. *U.S.P. XI* average dose 8 grains.

A yellowish-white crystalline powder, m.p. 74°. It is the ethyl ester of 6-methyl-2-phenylquinoline-4-carboxylic acid.

*Uses.* An analgesic, antipyretic and uric acid eliminant. Indicated in gout, rheumatism, arthritis, neuralgia, neuritis and sciatica. In acute rheumatic fever it is stated to be as efficient as the salicylates. It does not depress the heart, or injuriously affect the kidneys.

In rheumatic heart disease Tolysin has definite action, is less toxic than salicylates, and enables the worst cases of carditis to be treated without fear of drug complications.—F. J. Poynton, *Lancet*, ii/1928, 638.

Contrasted with control litter mates, no difference could be observed in the growth rate of young rats receiving daily for 100 days 1 g. per kilo of Tolysin. Histological evidence of liver damage in these animals is entirely lacking. Complete absorption of daily doses of this size in rats has been demonstrated. Tolysin in this enormous dosage has therefore no toxicity for rats. Similar dosage with cinchophen usually causes death within a few days or weeks, and even those which survive for many weeks exhibit very poor growth curves. Tolysin is far less toxic to rats than cinchophen, which fact accords with the extreme paucity of clinical evidence of Tolysin toxicity.—H. G. Barbour and A. Gilman, *J. Pharmacol.*, 1935, 55, 400.

## CINNAMOMUM

### B.P.

*Syn.* CANNELLE DE CEYLAN (*Fr. Cx.*).

*Dose.*—5 to 20 grains (0.3 to 1.2 g.).

The dried inner bark from *C. zeylanicum* (*Lauracæ*).

Aromatic, carminative and antiseptic, employed as flavouring agent. Contains volatile oil and tannin.

*P. Jap. V* has Cortex Cinnamomi *Loureirii*, *syn.* NIKKEI BARK, Japanese Cinnamon Bark. Cinnamomum *U.S.P. XI* is from *C. Loureirii*. *P. Helv. V* includes both Cortex Cinnamomi ceylanici

and chinensis, Ceylon cinnamon being used for the syrup, while other preparations are made from *C. Cassia* bark.

**Aqua Cinnamomi Destillata (B.P.).**

*Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.). 1 in 10.

**Aqua Cinnamomi Concentrata (B.P.).**

*Dose.*—5 to 15 minims (0.3 to 1 ml.).

Contains 2% *v/v* of oil of cinnamon, and is approximately 40 times the strength of the distilled water.

**Pulvis Cinnamomi Compositus (B.P.C.).** *Syn.* PULVIS AROMATICUS.

*Dose.*—10 to 60 grains (0.6 to 4 g.).

Cinnamon, ginger and cardamom, equal parts.

**Tinctura Cinnamomi (B.P.C.).**

*Dose.*— $\frac{1}{2}$  to 1 drachm. 1 in 5.

**Tinctura Cinnamomi Composita (B.P.C.).**

*Dose.*—1 to 2 drachms (4 to 8 ml.).

Cinnamon 1 in 40, with cardamom, long pepper and ginger.

**Oleum Cinnamomi (B.P., Fr. Cx.).**

*Dose.*— $\frac{1}{2}$  to 3 minims (0.03 to 0.2 ml.).

The light yellow oil distilled from the bark.

Contains 50 to 65% *w/w* of cinnamic aldehyde,  $C_9H_8O$ . *Fr. Cx.* requires 65 to 75%.

*Oleum Cinnamomi* (*U.S.P. XI, P. Jap. V*) is identical with *Oleum Cassiæ* (*B.P.C.*), from *C. Cassia*. It contains not less than 80% *v/v* of cinnamic aldehyde. *P. Helv. V* includes the oils from each of the two barks.

*Soluble* in alcohol 90% about 10 in 3.

**Uses.** Cinnamon oil is used in influenza and catarrhs, being given in milk or on sugar; is occasionally prescribed as an inhalation (30 to 40 minims) with boiling water 1 pint.

**Solutio Cinnamomi Composita (Brompton H.).**

Menthol 4, oil of cinnamon 3, oil of lemon 4, creosote 10, oil of pumilio pine 10, spirit of chloroform 10. For use on an oro-nasal respirator.

**Spiritus Cinnamomi (B.P.C.).** *Dose.*—5 to 20 minims (0.3 to 1.2 ml.). 1 in 10.

**Spiritus Cinnamomi (U.S.P. XI).** *Average dose.*—15 minims (1 ml.).

Oil of cinnamon (*U.S.P. XI, see above*) 10%, in alcohol.

**Cassia (B.P.).** *Syn.* CASSIÆ PULPA. *Dose.*—1 to 2 drachms (4 to 8 g.). The evaporated aqueous percolate of the pulp of commercial cassia pods. Mild aperient.

**Cassia Cortex.** *Syn.* CHINESE CINNAMON, CORTEX CINNAMOMI (*P. Jap. V*). Is the bark of *Cinnamomum Cassia* (Lauraceæ). It contains 1 to 2% of volatile oil. *Cassia Flos*, *syn.* CASSIA BUD, are the immature fruits, and are used as a spice.

**Cassia Fructus (B.P.C.).** *Syn.* CASSIA POD. The ripe fruits of *C. Fistula* (Leguminosæ). The fruit is a dark chocolate-brown pod about 35 to 50 cm. long and 18 to 25 mm. in diameter.

**Oleum Cassiæ (B.P.C.).**

*Dose.*— $\frac{1}{2}$  to 3 minims (0.03 to 0.2 ml.).

Obtained from the leaves and twigs of *Cinnamomum Cassia*. Resembles oil of cinnamon but has a less fragrant odour and a harsher taste.

**Canella (B.P.C.).** *Syn.* WILD CINNAMON. The bark of *Canella alba* (Canellaceæ) containing volatile oil. Stomachic.

**Oliveri Cortex (B.P.C.).** *Syn.* BLACK SASSAFRAS. From *Cinnamomum Oliveri* (Lauraceæ). Has been used as a substitute for cinnamon.

**Tinctura Oliveri Corticis.** *Dose.*— $\frac{1}{2}$  to 1 drachm. 1 in 10.

## COCA

(with COCAINE and COCAINE SUBSTITUTES)

B.P.C., Fr. Cx.

Syn. COCÆ FOLIA (P. Helv. V, P. Ital. V), CUCA.

[D] "Coca leaves," see p. 1143.

"Cocaine (including synthetic cocaine) and ecgonine and their respective salts, and the esters of ecgonine and their respective salts";

"Any solution or dilution of cocaine or its salts in an inert substance whether liquid or solid, containing any proportion of cocaine, and any preparation, admixture, extract or other substance (not being such a solution or dilution as aforesaid) containing not less than one-tenth per cent. of cocaine or of ecgonine."

"All preparations of esters of ecgonine or of their respective salts and all preparations of ecgonine containing less than one-tenth per cent. of ecgonine."

Note.—"Ecgonine" is used above to mean *lævo*-ecgonine, and includes any derivatives of ecgonine from which it may be recovered industrially.

[P1] "Alkaloids, the following; their salts, simple or complex:—Coca, alkaloids of."

"Amino-alcohols, esterified with benzoic acid, phenylacetic acid, phenyl propionic acid, cinnamic acid or the derivatives of these acids."

"Guanidines, the following:—Polymethylene diguanidines, di-para-amisylphenetyl guanidine."

"Orthocaine; its salts."

"Oxycinchonic acid, derivatives of; their salts; their esters."

"Para-amino-benzoic acid; esters of; their salts."

"Phenetidylphenacetin."

[S1] "Alkaloids, the following; their salts, simple or complex:—Coca, alkaloids of, except substances containing less than 0.1% of the alkaloids of coca."

"Amino-alcohols, esterified with benzoic acid, phenylacetic acid, phenyl propionic acid, cinnamic acid or the derivatives of these acids, except in substances containing less than 10% of esterified amino-alcohols."

"Guanidines, the following:—Polymethylene diguanidines, di-para-amisylphenetyl guanidine."

"Oxycinchonic acid, derivatives of; their salts; their esters."

"Phenetidylphenacetin."

Dose.— $\frac{1}{2}$  to 1 drachm (1. to 4 g.). Fr. Cx. gives maximum dose in 24 hours 8 g.

The dried leaves of *Erythroxylum Coca* (Bolivian or Huanuco Leaf) or of *E. truxillense* (Peruvian or Truxillo leaf) (Erythroxylaceæ).

The Bolivian leaves are browner, larger, broader and thicker; the veins are prominent; and there are clearly defined lines on each side of the midrib, which shows a distinct ridge in its centre.

Peruvian leaves are pale green, less oval and more elliptical in outline, and are much more fragile, being frequently broken.

The Bolivian leaves, imported from that country, are preferred for medicinal use, since a larger proportion of the alkaloids is cocaine. Java supplies most of the Truxillo variety. Ceylon was at one time a regular producer, but cultivation was abandoned at the request of the British Government. Coca is now frequently valued on its ecgonine content since commercial cocaine is obtained synthetically from ecgonine.

The total alkaloid content varies from 0.5 to 1.5%. Truxillo and Java leaf contains more, but only about 50% is cocaine. The total alkaloid of Bolivian leaf contains 70 to 80% of cocaine.

**Uses.** As a nerve and muscle stimulant, and of value in gastralgia, nausea and vomiting, and for the discomfort following excessive eating or drinking. Coca leaf chewing is extensively practised in Bolivia and Peru, 2 to 4 ounces being used per day. It staves off hunger and fatigue and gives stamina.

[P1] **Elixir Cocæ** (B.P.C.). *Dose.*—1 to 4 drachms (4 to 15 ml.) in water.

A palatable preparation containing 16½% v/v of liquid extract of coca equivalent to about 0.08% w/v of alkaloids; 4 dr. contains about ½ gr.

[D-P1-S1] **Extractum Cocæ.**

*Dose.*—2 to 15 grains (0.12 to 1 g.), in pills or pastilles. A dry extract, made with alcohol 60% and standardised to 2% of alkaloids (1 = about 4 of leaves).

[D-P1-S1] **Extractum Cocæ Liquidum** (B.P.C., Fr. Cx.). *Syn.* MISCELLIBLE LIQUID EXTRACT OF COCA.

*Dose.*—½ to 1 drachm (2 to 4 ml.). Standardised to contain 0.5% of ether-soluble alkaloids; 1 dr. contains about ½ gr. of coca alkaloids.

A single emergency dose of Extractum Cocæ Liquidum is said to be of value in cases of hæmorrhage due to piles when patient has to stand for any length of time.

[P1] **Vinum Cocæ** (Fr. Cx.). Macerate coca leaves 60 g. in "liqueur wine" 1000 g., for 10 days.

[D-P1-S1] **Cocaina** (B.P., F.E. VIII, P. Helv. V, U.S.P. XI, Fr. Cx.). *Syn.* METHYL-BENZOYLECAGONINE.

$C_9H_{13}(CH_3)(C_6H_5CO)NO_3 = 303.2$ .

*Dose.*—½ to ¼ grain (0.008 to 0.016 g.), in a pill or tablet. *Fr. Cx.* has max. single dose 0.05 g.; max. in 24 hours 0.15 g.

In shining monoclinic prisms, m.p. 97° to 98°. It is obtained from coca, and was first isolated by Niemann in 1860.

**Soluble** 1 in 10 of alcohol 90%, 2 in 1 of chloroform, about 1 in 4 of ether, 1 in 80 of light petroleum, 1 in 100 to 150 of liquid or soft paraffin, 1 in 10 of castor oil, 1 in 24 of olive oil, 1 in 2 of warm anhydrous wool fat; soluble in oil of clove and other volatile oils. Soluble 1 in 1300 of water and about 1 in 1000 of 1% sodium bicarbonate. Insoluble in glycerin.

**Antidotes.** (Acute poisoning.) Emetics will probably be useless, so empty stomach by stomach tube, using dilute solution of potassium permanganate or tannic acid. Give medicinal charcoal stirred up in water. (If the cocaine has been injected, obviously the use of the stomach tube and charcoal is useless.) Keep patient lying down and warm. Ammonia inhalations. Strychnine, ½ gr. hypodermically. Sodium Amytal, 3 to 10 ml. of 10% solution,

intravenously at rate of 1 ml. per minute, or chloroform, for convulsions. Nikethamide, 5 to 15 ml. of 25% solution, intravenously for circulatory collapse.

**Cocaine Addiction.** Cocaine fascinates by the rapidity with which it relieves exhaustion and dispels gloom by producing a delightful sense of mental and physical vigour. The stimulant effect is succeeded by a feeling of profound depression. Considerable tolerance is acquired by cocaine addicts, so that as much as 2 or 3 g. daily may be self-administered hypodermically. The discomforts caused by cocaine are readily controlled by morphine and when the patient learns this, the addiction becomes confirmed. Atropine, or better, hyoscine is the best for treatment of addiction.

Cocaine sniffed up the nose is readily absorbed. It first powerfully stimulates the brain and lassitude and fatigue pass, but a marked depression of the central nervous system succeeds. Frequent application to the nose causes perforation of the nasal septum.

**Uses.** For general uses of cocaine and its salts *vide* *Cocainæ Hydrochloridum*. The base is used for the preparation of oily solutions and ointments. A solution in olive oil has been used to anæsthetise the mucous membrane and allay cough in cauterising laryngeal growths.

A 2% solution in almond oil is mostly used for earache. For the eye a 2% solution in castor oil is used, sometimes combined with homatropine; for catheters, a solution in equal parts of castor and almond oils is useful.

1 or 2% in soft paraffin is suitable for eye work, and 4% or stronger is useful for catheterisation, burns, and for intense sensitiveness of parts, pruritus, etc.

[D-P1-S1] **Buginaria Cocainæ (B.P.C.)** contain  $\frac{1}{2}$  grain of the alkaloid. Useful in urethral affections.

[P1-S1] **Guttæ Cocainæ (B.P.C.)**. *Syn.* COCAINE EYE DROPS (FACTORY ACT, SOLUTION No. 1), FACTORY EYE DROPS.

For a foreign body in the eye.

Dissolve powdered cocaine (base) 0.5 g. in castor oil 95 g. on a water bath. While still warm add a solution of 0.033 g. of mercuric chloride in 1 ml. of dehydrated alcohol. Mix by rotating. Apply with a camel hair brush. (Exempt [D].)

The crystals which form on standing consist of benzoylecgonine and are produced by hydrolysis of the cocaine. The conditions necessary for maximum stability are the use of a good quality castor oil having a low acid value, a dry container and absence of water in the alcohol, and use of little or no heat.—W. Forster, *Pharm. J.*, ii/1936, 83.

[D-P1-S1] **Gutt. Cocain. c. Oleo (N.I.F.)**.

Cocaine 2 gr., castor oil to 2 dr. To be dissolved in the cold.

[D-P1-S1] **Nebula Cocainæ Composita (B.P.C.)** contains 0.5% w/v of cocaine in compound menthol and thymol spray.

[D-P1-S1] **Nebula Cocainæ Oleosa.**

Cocaine 1, oleic acid 4, liquid paraffin to 20.

[D-P1-S1] **Unguentum Cocainæ (B.P.C.)**. Cocaine 4%, as oleate, in lard. Useful where absorption is required, as in facial neuralgia, shingles, eczema, crysipelas, urticaria, and pruritus.

[D-P1-S1] **Cocainæ Hydrochloridum (B.P., U.S.P. XI, Fr. Cx., P. Helv. V, P. Dan., etc.)**.  $C_{17}H_{21}O_4N.HCl = 339.6$ .

*Dose.*— $\frac{1}{2}$  to  $\frac{1}{4}$  grain (0.008 to 0.016 g.), but more may be given,

in solution, pill or pastille. *Hypodermically*  $\frac{1}{4}$  to  $\frac{1}{2}$  grain (0.016 to 0.03 g.).

*Fr. Cx.* and *P.G. VI* give maximum single dose,  $\frac{3}{4}$  grain; maximum during 24 hours, 2  $\frac{1}{2}$  grains approx. *P. Ital. V* and *P. Helv. V*  $\frac{1}{2}$  and 1 grain respectively.

Shining, lamellar crystals, with bitterish taste. One part of cocaine base = 1.12 of the hydrochloride.

**Soluble** 2 in 1 of water, 1 in 3 of alcohol, also in glycerin; insoluble in ether, fats, and oils. It will crystallise with 9.5% of water of crystallisation, but the anhydrous salt is preferred. M.p. when placed in heating bath at 193°, not below 197°.

For a review of investigations into the loss of activity of solutions on keeping, see *Pharm. J.*, ii/1934, 501.

Conflicting results have been reported, but it appears to be desirable that the reaction of the solution should be about pH 5 before sterilisation.

**Incompatible** with ammonium carbonate (soluble in excess), phenol, mercuric and mercurous chlorides. It is also precipitated by borax.

When borax and cocaine hydrochloride are prescribed together, a weight of boric acid equal to that of the borax should be ordered at the same time to prevent precipitation.

In dispensing ammoniated mercury with cocaine hydrochloride in the form of an ointment, dissolve the cocaine salt in a drop or two of water. Rub the ammoniated mercury down with a little almond oil, mix, and add the remainder of the ointment base—e.g., soft paraffin.

With phenol, cocaine hydrochloride is compatible in presence of glycerin or alcohol, but not in aqueous solutions.

### **Uses of Cocaine and its Salts.**

Cocaine is a powerful local anæsthetic, paralysing the sensory nerve fibres and causing local vasoconstriction. It renders the superficial structure of the eye anæsthetic, is a mydriatic, and paralyses the accommodation. Applied to mucous membrane it blanches the part, simultaneously producing anæsthesia. The anæsthetic action of cocaine may be prolonged by the addition of adrenaline solution. Application of an ointment (alkaloid) will remove the pain of eczema, erysipelas, facial neuralgia or shingles, and the irritation of urticaria or pruritus.

For burns and scalds, brush with a 4% aqueous solution (hydrochloride) and apply cocaine ointment on cotton wool or lint; for fissured nipples and insect bites, apply an aqueous solution; for hay fever, influenza, coryza, bronchitis, spasmodic asthma, laryngitis and pharyngitis, a spray of an aqueous solution to relieve irritability of mucous surface. Spasmodic and painful affections of the vagina may be minimised by vaginal injections of  $\frac{1}{4}$  grain in 1% oily solution; rectal and prostatic pains are relieved by  $\frac{1}{2}$ -grain suppositories. In the urethra a solution exceeding 1% should not be used. A rectal injection checks diarrhoea and dysentery.

**IN DENTISTRY.** For extraction, 1 ml. of 1 to 2% solution is used with the addition of  $\frac{1}{2}$  to 1 minim of solution of adrenaline hydrochloride. For plugging, preparations such as 10% cocaine in lanolin or Cocaine-Menthol-Eugenol are used.



Much of the ill-effect formerly thought to be due to cocaine is now realised to be due to adrenaline. For dental extraction and conservative work strengths of from 1 in 50,000 to 1 in 75,000 are sufficient. Too much adrenaline in the solution may cause delayed hæmorrhage.—H. T. Roper-Hall, *Dental Gazette*, Sept. 1939, 26.

**FOR SMALL OPERATIONS.** Solutions of cocaine hydrochloride have been used in excision of the tonsils, cauterising the turbinated tissue of the nose, painting chancres previous to the application of caustics, removing polypi, iridectomy and operation for cataract, squint, and the removal of foreign bodies from the eye. For the eye aqueous solutions of cocaine hydrochloride 2 to 4% strength and for other purposes 4 to 50%; it is necessary to repeat the application of the weaker solutions. No operation should be commenced within at least 10 minutes of the first application. Injurious effects, either local or constitutional, rarely follow its use.

**FINGER AMPUTATION.** Cocaine solution 5%, to which 5 m. of liquefied phenol and 5 m. of solution of adrenaline hydrochloride have been added to each ounce of the solution: never exceeding 90 m., often less.

**NOSE, THROAT AND EAR OPERATIONS.** The *nose* may be plugged with strips of gauze soaked in 10 to 20% cocaine solution, to which a few drops of 1 in 1000 adrenaline have been added. None of the synthetic local anæsthetics equal cocaine when applied to mucous membrane. Operations should be preceded by morphine and atropine hypodermically. In nose operations *adrenaline* should be applied followed by cocaine, injection being made slowly.

In *throat* operations a 5 to 10% solution should be applied first.

For *ear* operations as local anæsthetic. Cocaine hydrochloride, menthol, phenol, clove oil, and rectified spirit, equal parts.

A useful and safe solution of cocaine for local anæsthesia of the nose is one containing 34% cocaine, 1 in 1000 adrenaline solution, 2% potassium sulphate. The potassium sulphate solution acts as a catalytic agent, and the anæsthesia to be expected from a 15% solution of cocaine is attained.

Local anæsthesia of the pharynx or larynx may readily be induced by the application of cocaine and adrenaline on cotton-wool applicators. For the pharynx 10% solution of cocaine with one-fifth part of adrenaline solution can be used. For the larynx 20% with one-fourth part of adrenaline solution is used.—F. C. Ormerod, *Practitioner*, i/1937, 528.

**ENUCLEATION OF THE TONSIL** under local anæsthetic. For surface anæsthesia a mixture of equal quantities of 10% cocaine hydrochloride solution and adrenaline solution used, applied with cotton swabs, and repeated three or four times, followed by infiltration of the tissues in which the tonsil lies embedded with a 5% Novocain solution.

**INTRASPINAL ANÆSTHESIA.** Cocaine hydrochloride has been used for *intraspinal anæsthesia* using  $\frac{1}{2}$  to 2% solution, but it is generally considered too toxic for this purpose.

**LOCAL INFILTRATION ANÆSTHESIA** is produced by 0.1 to 0.2% solutions of cocaine with a small quantity of adrenaline solution. Its action commences in three minutes, increases for ten to twenty

minutes, and mostly disappears within half an hour. The anæsthesia may be prolonged by applying a triangular bandage when possible above the site of injection; this has also the advantage of lessening the risk of toxic symptoms, as the delay of cocaine in the tissues renders it innocuous.

[D·P1·S1] **Auricular Cocainæ Hydrochloridi.** Ear cones, contain  $\frac{1}{10}$  gr. in each with oil of theobroma basis.

[D·P1·S1] **Guttæ Cocainæ (R.L.O.H.).** Cocaine hydrochloride 8 or 16 gr. to 1 oz.

[D·P1·S1] **Guttæ Cocainæ cum Adrenalina.**

Cocaine hydrochloride 5% in solution of adrenaline hydrochloride.

[D·P1·S1] **Injectio Cocainæ et Sodii Bicarbonatis.** Cocaine hydrochloride  $\frac{1}{2}$ , sodium bicarbonate  $\frac{1}{2}$ , chlorbutol  $\frac{1}{2}$ , distilled water to 100.

*Dose.*— $\frac{1}{2}$  to 4 drachms (8 to 15 ml.) for *urethral injection*.

This solution is remarkably efficacious for use prior to passing a catheter.

[D·P1·S1] **Lamellæ Cocainæ (B.P.).** DISCS OF COCAINE.

Discs of gelatin, each containing  $\frac{1}{10}$  gr. of cocaine hydrochloride, are for ophthalmic use. Also prepared containing  $\frac{1}{10}$  gr. in each in combination with atropine sulphate (*q.v.*), and homatropine (*q.v.*).

[D·P1·S1] **Isotonic Cocaine Eye Lotion.**

Cocaine hydrochloride 1, sodium chloride 1·25, distilled water to 100. This is isotonic with the tears.

[D·P1·S1] **Mixtura Cocaini (Fr. Cx.).** *Syn.* BONAIN'S ANÆSTHETIC MIXTURE, SOLUTIO BONAIN (T.H.).

Cocaine hydrochloride, phenol and menthol, equal parts.

[D·P1·S1] **Nebula Cocainæ Composita.** Cocaine 2 gr., cinnamon oil 5 m., menthol 15 gr., liquid paraffin to 1 oz.

[D·P1·S1] **Nebula Cocainæ Hydrochloridi.** May be prepared 1, 5 or 10%, or more if ordered, with sterile normal saline for general use.

[D·P1·S1] **Oculentum Cocainæ (B.P.)** contains 0·25% of cocaine hydrochloride.

[P1] **Pastilli Cocainæ Hydrochloridi (B.P.C.)** contain  $\frac{1}{10}$  gr. (0·0016 g.).

To allay throat irritation and hoarseness.

[D·P1·S1] **Pigment. Cocain. Co. (P.M.H.).** Dilute ointment of mercuric nitrate 30 gr., menthol 2 gr., oil of lavender 10 m., cocaine hydrochloride 6 gr., olive oil to 1 oz.

[D·P1·S1] **Pigmentum Cocainæ et Hydrargyri Perchloridi.** Cocaine hydrochloride 28 gr., solution of mercuric chloride 20 drops, glycerin 4 dr., water 4 dr., after syringing ears twice or thrice daily with boric acid lotion.

Of value for painting the external auditory meatus and membrana tympani.

[D·P1·S1] **"Cocaine-Menthol-Eugenol."** Cocaine, menthol, eugenol and alcohol 90% equal parts. Applied on a pledget of cotton wool, followed by jets of cold air, *e.g.*, from a chip syringe, relieves toothache rapidly.

[D·P1·S1] Camphor 5, chloral hydrate 5, cocaine hydrochloride 1, warmed, form an oily liquid which cures toothache.

[D·P1·S1] **Suppositories and Pessaries**  $\frac{1}{2}$  grain (0·03 g.), or more.

[D·P1·S1] **Compound Cocaine Suppository** of cocaine hydrochloride  $\frac{1}{2}$  gr. with morphine hydrochloride  $\frac{1}{2}$  gr. is useful for painful hæmorrhoids.

[D·P1·S1] **Tabellæ Cocainæ.**  $\frac{1}{10}$ ,  $\frac{1}{20}$ , and  $\frac{1}{30}$  grain with chocolate. The usual dose is  $\frac{1}{30}$  grain.

*Dose.*—1 every quarter, half-hour or hour, quickly eaten and swallowed. Useful for sea-sickness, chloroform or alcoholic sickness, and that of pregnancy.

Sea-sickness may be overcome by internal use of the following:—Cocaine hydrochloride 0·2 g., iodine tincture 2 ml., water to 150 ml. *Dose.*—1 tablespoonful 2 to 4 times daily. More palatable without the iodine.

[D·P1·S1] **Trochisci Cocainæ Hydrochloridi (T.H.).**  $\frac{1}{30}$  grain (0·006 g.) in each. *Brompton H.* has  $\frac{1}{8}$  grain in 20 grains.

[D-P1-S1] **Codrenine** (*Parke, Davis, London*). Cocaine hydrochloride 2% and adrenaline chloride 1 in 15,000. *Dose*.—For dental extractions 8 minims. Local anæsthetic.

[D-P1-S1] **Locosthetic** (*Parke, Davis, London*). Cocaine hydrochloride 0.75% with adrenaline chloride 1 in 50,000. Analgesic for use in dentistry. Locosthetic Modified is similar with 1 in 100,000 of adrenaline chloride.

[D-P1-S1] **Sterilocaine** (*Pharmaceutical Manufacturing Co., London*). Self-sterilising local anæsthetic solution containing cocaine hydrochloride 0.95%, adrenaline 0.00125%, with quinine derivatives and thymol in Ringer's solution.

[D-P1-S1] **Cocainæ Nitras** (*P.G. VI, P. Helv. V*).  
 $C_{17}H_{21}O_4N \cdot HNO_3 = 366.2$ . (*Fr. Cx.* has  $2H_2O$ .)

*Dose*.— $\frac{1}{4}$  to  $\frac{1}{2}$  grain (0.008 to 0.016 g.).

In large colourless crystals, readily soluble in water. Is compatible with silver nitrate, and if used previously in solution lessens the pain caused by the latter salt.

[D-P1-S1] **Cocainæ Salicylas**.  $C_{17}H_{21}O_4N \cdot C_6H_4(OH) \cdot COOH = 441.2$ .  
*Dose*.— $\frac{1}{4}$  to  $\frac{1}{2}$  grain (0.008 to 0.016 g.).

In white deliquescent masses; it forms a solution which keeps well. Soluble 5 in 1 of water,  $2\frac{1}{2}$  in 1 of alcohol 90%. In spasmodic asthma, the hypodermic injection of a full dose at the beginning relieves the attack.

[P1-S1] **Tropacocainæ Hydrochloridum** (*P.G. VI, P. Jap. V*).  
*Syn.* BENZOYL PSEUDOTROPINE HYDROCHLORIDE.

$C_9H_{14}ON \cdot C_6H_5CO \cdot HCl = 281.6$ .

The salt of the base tropacocaine obtained from Java coca, or synthetically. In white crystals, m.p.  $271^\circ$ . Freely soluble in water. Aqueous solutions keep well and can be boiled with impunity.

*Uses*. Is a powerful anæsthetic; in the eye causes neither ischæmia nor irritation of hyperæmia. 3% solution recommended; anæsthesia is produced more quickly than with cocaine but is more transitory; the action may be kept up by adding a drop from time to time. Mydriasis occurs occasionally but is slight. Severe sciatica has been treated successfully by injecting 1 ml. of 5% solution into the dural sac in the lumbar region.

The 5% solution has been used for intraspinal anæsthesia, the dose for a healthy person weighing 11 stones being 20 m., a further 8 to 12 m. being given 40 to 50 minutes later if required.

**Erythrophloeum**. *Syn.* CASCA BARK, SASSY BARK, ORDEAL BARK. The bark of *Erythrophloeum guineense* (*Leguminosæ*). Contains the alkaloid erythrophloein which has a digitalis action and is also anæsthetic.

**Tinctura Erythrophloei**. 1 in 10 of alcohol 90%. *Dose*.—5 to 10 minims.

**Erythrophloeinæ Sulphas**. *Dose*.— $\frac{1}{16}$  to  $\frac{1}{8}$  grain in pill. Yellowish granular crystals, very soluble in water. Has the combined action of digitalin and picrotoxin, and is a local anæsthetic for eye work in 0.05 to 0.25% solution, also as a dental obtundent in 50% solution in eugenol.

[P1-S1] **Amydricainæ Hydrochloridum** (*B.P.C.*). *Syn.* BENZOYL TETRAMETHYLDIAMINODIMETHYLETHYL CARBINOL HYDROCHLORIDE (*P.G. VI*). (Formerly issued under the proprietary name ALYPIN.)  $C_9H_5 \cdot COOC(C_2H_5)[CH_2N(CH_3)_2]_2 = 314.7$ .

*Dose*.— $\frac{1}{16}$  to  $\frac{1}{8}$  grain (0.003 to 0.03 g.) *per os*.

White, crystalline powder melting at about  $169^\circ$ . *Soluble* 1 in 1 of water and 1 in 4 of alcohol 90%.

*Uses*. Solutions containing 0.025 to 0.5% or up to 10% are efficient in eye work. (Strong solutions keep well, but weak ones may become cloudy; they may be sterilised by boiling, but not

longer than five minutes.) 2% strength produces insensibility of cornea in sixty seconds. It produces no mydriasis nor any disturbance of accommodation. Its toxicity equals that of cocaine and it is more irritant.

For lumbar anæsthesia injection of  $\frac{1}{2}$  to 1 ml. of 2% solution has been used. For infiltration 0.01 to 0.1% solution has been used with same quantities of cocaine hydrochloride in 0.2% sodium chloride solution.

Internally in sickness and post-operative vomiting it acts like cocaine.

[P1-81] **Amylocainæ Hydrochloridum** (B.P., P. Ital. V, P. Belg. IV, P. Argent. II, F.E. VIII). *Syn. and Prop. Name.* CHLORHYDRATE D'AMYLÉINE (Fr. Cx.), STOVAINE (Pharmaceutical Specialities (May & Baker) Ltd., London).

$C_6H_5 \cdot CO_2 \cdot C(CH_3)(C_2H_5) \cdot CH_2N(CH_3)_2 \cdot HCl = 271.6$ .

*Dose.*—Per os and hypodermically,  $\frac{1}{4}$  to  $\frac{3}{4}$  gr. (0.02 to 0.05 g.). By intrathecal injection,  $\frac{1}{2}$  to 1½ grain (0.02 to 0.1 g.). Fr. Cx. has maximum single dose 1½ gr. approx., maximum in 24 hours 2½ gr. approx. P. Belg. IV gives 5 and 10 gr. approx. respectively.

In small white crystals, melting at 177° to 179°. Consists of the hydrochloride of the benzoyl ester of methylethyldimethylaminomethylcarbinol. Soluble 1 in 2 of water, 1 in 3 of dehydrated alcohol; readily soluble in methyl alcohol; almost insoluble in ether.

*Uses.* Amylocaine hydrochloride is a local anæsthetic. Its toxicity is only about half that of cocaine, but it is much more irritant and is inferior to cocaine for application to mucous membranes. It has been used similarly to cocaine for minor surgical operations, but its chief value is as a regional and spinal anæsthetic (*vide infra*).

ANGINA PECTORIS. Injection of 10 ml. of 1% Stovaine solution under the skin at the site of the most severe pain gave definite relief, when nitrites, etc., had failed. Valuable in patients with angina pectoris due to coronary spasm. —Brit. med. J. Epit., ii/1931, 7.

[P1] **Unguentum Adrenalinae et Amylocainæ Compositum** (B.P.C.).

Adrenaline 1 in 14,000, amylocaine hydrochloride and benzocaine 1% with liquid extract of hamamelis in wool fat and yellow soft paraffin. A valuable soothing ointment for hæmorrhoids.

### Intraspinal Anæsthesia with Amylocaine Hydrochloride.

The advantages of intraspinal anæsthesia are absence of post-operative shock, complete muscular relaxation, no venous engorgements or respiratory movements, no starvation, and no post-operative sickness. It is contraindicated in cases of advanced sepsis, in the presence of organic disease of the spinal cord or brain, and in very low blood pressure.

The canal is punctured between the second and third lumbar interspaces, the patient being in a sitting posture with the head and shoulders bent forward. 5 ml. of fluid is allowed to escape and then the injection made. Anæsthesia is produced within ten minutes, and lasts for about an hour.

By carefully adjusting the curves of the spine, either a high or low anaesthesia can be produced by gravitation. The lowering of the head in any operation is not favoured. The best results are obtained by not altering the level of the body after injection, except in cases of the labouring class advanced in life, where the spinal column may be almost rigid—here the pelvis may have to be raised. Usually 5 to 10 ml. of cerebrospinal fluid is withdrawn before injection. Any alteration of posture may be made providing the relative levels of head and pelvis remain as before.

To prevent shock following intraspinal anaesthesia, after removal of 5 to 10 ml. of spinal fluid and the injection of the anaesthetic, the spinal fluid is injected intravenously at the bend of the elbow and the operation commenced 5 or 6 minutes later.

For the production of spinal anaesthesia various solutions are employed, those most commonly used being (1) "Heavy" solution (Barker's solution), (2) Chaput's solution, and (3) "Light" solution—Stovaine 5% in normal saline. The terms "light" and "heavy" are misleading, however, and unless the solution has the same specific gravity as the cerebrospinal fluid, *i.e.*, approximately 1.007, gravitational diffusion will occur.

[P1] **Barker's Solution.** Stovaine 0.1 g., dextrose 0.1 g., sterilised water to 2 ml. Sp. gr. 1.025. Dose.—1 ml. Often the dose may be reduced to 0.8 ml., sometimes increased to 1.2 ml.

Using this solution, a small dose of the drug can be employed and the severest operations performed. The equivalent of 0.06 g. of Stovaine is usually found to be sufficient. As a rule anaesthesia is established in 5 to 7 minutes for the groins and 8 to 10 for the epigastrium. There is almost always pyrexia but no post-operative shock. Highest analgesia—clavicles.

Caffeine, 2 gr. hypodermically, should be given as soon as Stovaine has been administered, to counteract the fall in blood pressure; a second dose should be kept ready in case of emergency (the two "danger periods" are immediately after injection and 20 minutes later); pituitary extract a satisfactory substitute. Let the maximal dose of Stovaine solution be 0.8 ml.—Hamilton Bailey, *Practitioner*, i/1927, 372.

Other solutions used are the following:—

[P1] **Solutio Stovainæ et Glucosæ (St. T. H.)** contains 2½ or 5% with dextrose (anhydrous) 2½ or 5%.

[P1-81] **Chaput's Solution.** *Syn.* TUFFIER'S SOLUTION (*M.R.I.*). Stovaine 0.1 g., sodium chloride 0.1 g., sterilised water to 1 ml. Sp. gr. 1.080.

[P1] **Kroenig's Solution (M.R.I.).** Stovaine 0.08 g., sodium chloride 0.0022 g., water to 2 ml.

[P1] **Chaput's Alcohol Solution (M.R.I.).** Stovaine 0.08 g., alcohol 95% 0.2 ml., sterilised water to 2 ml.

These solutions are sometimes preferred because they diffuse more readily than the solution containing dextrose.

[P1] **Jonnesco's Stovaine Caffeine Solution** contains from 0.02 to 0.05 or 0.1 g. of Stovaine with caffeine 0.5 g. and sodium benzoate.

[P1] **Duplas' Solution (M.R.I.).** Stovaine 0.06 g., caffeine 0.1 g., sodium benzoate 0.1 g., sterilised water to 2 ml.

Caffeine is included in these formulæ to counteract the fall in blood pressure, and is preferred to strychnine, which was at one time advocated for the purpose by Jonnesco.

### Combined Spinal and Splanchnic Anaesthesia.

For abdominal operation in the neighbourhood of the diaphragm, spinal anaesthesia with 0.1 g. of Stovaine (between the second and

third lumbar vertebræ), combined with splanchnic anæsthesia with 60 to 70 ml. 0.5% solution of procaine hydrochloride, given according to Braun's method, is the anæsthetic of choice. In operations lasting over an hour spinal anæsthesia alone is not sufficient. Anæsthesia may be prolonged by a further dose of splanchnic anæsthetic and infiltrating the peritoneal and abdominal muscles with 0.5% procaine hydrochloride in 1 in 200,000 adrenaline solution. In nervous patients, a dose of bromethol per rectum produces quiet sleep. The combination gives complete and uniform muscular relaxation and reduces diaphragmatic movements to a minimum.

[P1-S1] **Benzamine Hydrochloridum** (B.P.C.). *Syn. and Prop. Name.* BETACAINE HYDROCHLORIDE, BETA-EUCAINE HYDROCHLORIDE (*Schering, London*), EUCAINE HYDROCHLORIDE (U.S.P. XI), 4-BENZOYLOXY-2:2:6-TRIMETHYLPYPERIDINE HYDROCHLORIDE.  $C_8H_7N(CH_3)_3(C_6H_5COO) \cdot HCl = 283.6$ .

*Dose.*— $\frac{1}{2}$  to  $\frac{1}{2}$  grain (0.008 to 0.03 g.) or more.

A white crystalline synthetic compound allied to cocaine, *soluble* about 1 in 30 of water (crystals may deposit on cooling but can be redissolved without harming the salt), 1 in 35 of alcohol 90% and 1 in 6 of chloroform at 25°. 2% solutions are used in ophthalmic work. Solutions may be boiled without decomposing the salt.

A local anæsthetic possessing only about half the toxicity of cocaine, but with slighter anæsthetic effect and greater irritation. It does not dilate the pupil and it renders the tissues hyperæmic.

**Local Infiltration Anæsthesia** (*Barker*) with benzamine hydrochloride is suitable for very short operations using a solution of benzamine hydrochloride 3 gr. (0.2 g.), sodium chloride 12 gr. (0.8 g.), and water to 3½ oz. (100 ml.). This is isotonic.

The solution is boiled and on cooling 10 m. of adrenaline solution may be added. In the operation 50 ml. or more (up to 100 ml.) is injected all round the region to be dealt with.

[P1] **Nebula Benzaminæ.**

Benzamine hydrochloride 10 gr., sodium sulphate 4 gr., distilled water to 1 oz.

[P1] **Pastilli Benzaminæ** (B.P.C.) contain  $\frac{1}{2}$  gr. (0.03 g.).

[P1] **Unguentum Benzaminæ.**

Benzamine hydrochloride 1, olive oil 2, hydnous wool fat 7. For pruritus, menthol 2% may be added.

[P1-S1] **Beta-Borocaine** (*British Drug Houses, London*). Benzamine borate,  $C_{14}H_{21}O_2N_3HBO_2$ . *Dose.*— $\frac{1}{2}$  grain (0.025 g.). A surface anæsthetic recommended especially for ear, nose and throat work. Borocaine (*q.v.*) is preferred for injection.

For operative work on the eye, a 0.25% solution is recommended, and for operations on and examinations of the urethra and bladder in general a 0.5% solution is suitable.

It has three times the anæsthetic action on the rabbit's cornea, and  $\frac{1}{10}$  the experimental toxicity of cocaine hydrochloride. It is mildly irritant, causes some congestion, especially in the nose, and in very large doses excites the central nervous system.

[P1-S1] **Beta-Borocaine Tablets** contain 0.025 g., with adrenaline 0.00005 g., sodium chloride and cane sugar *q.s.* One dissolved in 10 ml. makes a 0.25% solution; 1 in 5 ml. makes a 0.5% solution.

[P1-81] **Benzaminæ Lactas** (B.P.C.). *Syn.* EUCAINE LACTATE, BENZACAINE LACTATE.  $C_{15}H_{21}O_2N, C_2H_5O_3 = 337.2$ .

*Dose.*— $\frac{1}{8}$  to  $\frac{1}{2}$  grain (0.008 to 0.03 g.).

A white crystalline salt with m.p.  $152^\circ$  to  $156^\circ$ .

*Soluble* about 1 in 5 of water and about 1 in 8 alcohol (90%).

*Incompatible* with salicylic acid.

For ophthalmic work and in dentistry employ 2 to 3%; for infiltration 0.1% with sodium chloride 0.8%; for regional anæsthesia 2.5%; nose, throat and ear 10 to 15%; for urethral injection, 1 to 2% solutions may be used to relieve pain. Solutions can be boiled.

It is slower in action than cocaine, is less toxic, and anæsthesia is more prolonged, while the heart is not affected, nor the pupil dilated.

Sciatica has been treated by injections.

[P1] **Benzocaina** (B.P.). *Syn. and Prop. Name.* ETHYL *p*-AMINO-BENZOATE (U.S.P. XI, P.G. VI, P. Helv. V, P. Dan., P. Ned. V, F.E. VIII, P. Belg. IV), ANÆSTHESIN (Bayer Products, London).  $NH_2 \cdot C_6H_4 \cdot CO_2 \cdot C_2H_5 = 165.1$ .

*Dose.*—5 to 10 grains (0.3 to 0.6 g.) in powder or cachets. U.S.P. XI average dose 5 grains. (The Council on Pharmacy and Chemistry of the A.M.A. does not approve of its internal use.)

White crystalline powder, m.p.  $90^\circ$  to  $91^\circ$ , with slightly bitter, numbing taste.

*Soluble* 1 in about 2500 of water, 1 in 8 of alcohol 90%, 1 in 4 of ether, 1 in 2 of chloroform, 1 in 50 of almond oil, 1 in 35 of olive oil.

*Uses.* A surface anæsthetic in powder form for dusting on wounds and injured surfaces; it rapidly paralyses sensory nerve endings. Internally it may be given in a dose of 3 to 5 gr. several times daily before meals to relieve the pain of gastric ulcer and carcinoma. Local insufflations sometimes with equal amount of orthocaine for pharyngeal and laryngeal affections; bougies 3 grains for urethritis, and suppositories 10 grains for hæmorrhoids. Ointments 10% for burns, eczema and intertrigo.

Pneumococcic (and tuberculous) infection of the throat, in a case of difficulty in swallowing, has been greatly relieved by applications of benzocaine dissolved in palm oil—in form of a spray.

Great relief of pain in inoperable carcinoma of the rectum from suppositories of benzocaine 5 gr. and acetylsalicylic acid 10 gr.—D. G. Greenfield, *Brit. med. J.*, ii/1932, 1041.

[P1] **Injectio Benzocainæ.** *Syn.* A.B.A.

Benzocaine 3, benzyl alcohol 5, and ether 10, in sterile olive oil q.s. to 100.

Has been widely used in the treatment of pruritus ani, pruritus vulvæ, and anal fissure.

In pruritus ani 10 ml. may be safely used at the first treatment—injected in relation to the posterior half of the perianal region through 4 punctures,  $2\frac{1}{2}$  ml. at each point. A week later 5 ml. is given by 2 punctures, and again another dose after a further week. In the average case, 3 doses—10, 5, and 5 ml.—suffice.

Permanent relief of pruritus ani from subcutaneous injections (round the anal margin) of either Benacol—a solution of equal parts of benzocaine and benzyl alcohol in 90 parts of almond oil, or A.B.A. as above. 4 ml. of either may be injected at a time and repeated at 3 to 7-day intervals, till the entire perianal region has been injected, 8 ml. being the average total injected. No general reaction or complications. Also gives rapid and brilliant cure in recent anal fissure.—W. B. Gabriel, *Brit. med. J.*, i/1929, 1071.

A.B.A. valuable for ano-rectal complaints—better than Novocain.—P. Kennedy Murphy, *Brit. med. J.*, ii/1930, 162.

Large doses of both oily and aqueous solutions as anæsthetics in pain and fissure should be avoided.—P. Kennedy Murphy, *Brit. med. J.*, ii/1930, 498.

Anal fissure treated by 2 to 5 ml. of A.B.A. injections into the sphincter.—W. J. Lytle, *Brit. med. J.*, i/1931, 498.

Pruritus ani and anal fissure, and spasm of the sphincters, treated by A.B.A. Pain relieved instantly.—Arthur S. Morley, *Brit. med. J.*, ii/1930, 80.

Percaine (see p. 439) 0.5%, benzyl alcohol 10%, phenol 1%, in 5 ml. of sterile oil, also used instead of the above. For anal fissure A.B.A. 5 ml., or the Percaine in oil (5 ml.) will reduce sphincteric relaxation. Local anæsthetic effect lasts as long as 10 days.—W. B. Gabriel, *Brit. med. J.*, ii/1930, 311.

Percaine in oil (made up according to Gabriel's formula) is the most satisfactory local anæsthetic in hæmorrhoidectomies; anæsthesia lasts from 7 to 10 days. Contraindications are local infection, eczema and a possible idiosyncrasy.—N. J. Simmons, *New Engl. J. Med.*, 1936, 214, 20.

45 cases of anal fissure treated with A.B.A. 18 healed after one injection, and 4 after two. In another 14 it can be assumed that in most, if not all, the fissure healed. The important point, however, is that many cases do not heal in spite of repeated injection.—J. W. Riddock, *Lancet*, ii/1936, 1150.

RECTAL ANÆSTHESIA. A.B.A. and the Percaine solution both found to give rise to pain on injection and very often to severe pain several hours afterwards. The following formula is an improvement: Procaine base 1.5%, butyl-paraminobenzoate 6%, benzyl alcohol 5%, in sterilised almond oil. Its advantages are its certainty of effect, painlessness on injection (if given slowly), freedom from severe after-pain, anæsthesia or hypoaesthesia produced for periods up to 28 days or longer. It is comparatively non-toxic; 20 to 30 ml. may be injected without ill-effect and with no local reaction. The solution, first warmed, is injected into the deeper tissues at the inner boundary of the ischio-rectal fossæ as well as into the more subcutaneous plane. On no account should an injection be given in the presence of acute sepsis, and when there are excoriations the needle must be inserted through clean normal skin. Good results in the treatment of fissure-in-ano (5 to 10 ml. average amount injected) and pruritus ani (from 15 to 30 ml. injected at one time).—C. N. Morgan, *Brit. med. J.*, ii/1935, 938.

PRURITUS VULVÆ. Though A.B.A. does not cure the condition, it affords a long relief, enabling septic scratches to heal and the patient to gain much-needed rest.—A. Bourne, *Practitioner*, ii/1933, 441.

Of 15 patients treated 5 were cured, 5 much improved, 4 slightly improved and 1 not improved. Weekly injections of 2 ml. just beneath the skin in such manner that a fan-shaped area is treated, a different zone being dealt with at each visit, until eventually the whole vulvar region has been infiltrated. The number of injections varied from 3 to 33.—C. W. Kennedy, *Edinb. med. J.*, Sept., 1933, 125.

[P1] Sterules B.A.B.A.N. (*Martindale, London*) contain 5 ml. of an alcohol-oil solution of Butesin and benzocaine with 1% of procaine base.

The addition of 1% of basic Novocain as in B.A.B.A.N., is a distinct improvement; a more immediate effect is noted after its injection, and also an excellent late anæsthetic effect is developed; pain after injection is usually absent. In anal spasm and fissure the deep injection of 5, or sometimes 10 ml., of A.B.A. or B.A.B.A.N. into the external fissure has proved of great value. In acute anal fissures a preliminary injection, from a posterior puncture, of 10 ml. of Novocain into the sphincter, on each side of the middle line, is often helpful. In pruritus ani, if palliative treatment fails to relieve the irritation, and in the absence of any local cause, subcutaneous injections of A.B.A. or B.A.B.A.N. are of value, giving 3 injections of 10 ml. at 5 to 7 day intervals. These injections should not be given in the presence of an acute moist dermatitis, and good results are unlikely if the pruritus extends forward to the vulva.—W. B. Gabriel, *Practitioner*, ii/1934, 497.



[P1] **Pigmentum Benzocainæ cum Menthol** (*Brompton H.*).

Menthol 24 gr., acacia 2½ dr., almond oil 2½ dr., water 2½ dr.; emulsify, and add benzocaine 90 gr., alcohol 90%, 10 dr., water 2 oz.

Painted on the larynx affords relief in tuberculosis of the larynx.—Sir James Dundas Grant, *Practitioner*, ii/1931, 260.

[P1] **Unguentum Benzocainæ (Nasal)** (*J.H.*).

Benzocaine 20 gr., ephedrine hydrochloride 5 gr., solution of adrenaline 15 m., eucalyptol 5 m., soft white paraffin to 1 oz.

[P1] **Anesthose Cream** (*Parke, Davis, London*). Benzocaine, adrenaline chloride and ephedrine hydrochloride in lanolin and soft paraffin base. Anæsthetic and astringent; gives relief in hay fever and is a palliative in allaying irritation, congestion and inflammation of the nasal mucous membrane.

[P1] **Cycloform Ointment** (*Bayer Products, London*). Alkyl ester of para-aminobenzoic acid 10%, with extract of hamamelis and zinc oxide. Analgesic, antiseptic and astringent; for hæmorrhoids, pruritus, burns, eczema, etc.

[P1] **Larysept** (*Richter, London*). Tablets containing benzocaine ¼ gr., butyl-aminobenzoylethylmethylaminoethanol hydrochloride (*see* Butethanol) 100 gr., formalin ½ m., menthol ⅞ gr. *Dose*.—1 tablet dissolved in the mouth every three hours. An antiseptic and analgesic in laryngitis, pharyngitis, etc.

[P1] **O-R-92** (*Medico-Chemical Corporation, New York; Coates & Cooper, London*). Lozenges for use in throat affections containing the ethylbutyl ester of dicarboxydiphenylmethaneacridoni-oxyquinoline, with borax, potassium sulphate and benzocaine.

[P1] **Proctocaine** (*Allen & Hanburys, London*). Procaine base 1.5%, butyl-*p*-aminobenzoate 6%, benzyl alcohol 5%, in sterilised almond oil. *Dose*.—1 to 5 ml. repeated if necessary at intervals of a week or more. For rectal anæsthesia in anal fissure, pruritus ani, etc.

When using oil-soluble anæsthetics such as Proctocaine in rectal surgery it is of paramount importance to use them *before* the operation for fissure or hæmorrhoids is actually commenced, and to be meticulous in the aseptic technique of injection in order to avoid abscess formation and the spreading of infection. Not infrequently rectal pain due to a small submucous abscess is treated by injection of an oil-soluble anæsthetic in the belief that the patient has an uncomplicated fissure. The results are disastrous. Injection must not be given in the presence of infection or in cases of unproved diagnosis.—C. N. Morgan, *Practitioner*, ii/1939, 515.

[P1] **Risin** (*Coates & Cooper, London*). Ointment containing benzocaine, adrenaline, menthol, eucalyptol, boric acid and soft paraffin and wool fat. Catarrh, hay fever, etc.

[P1] **Butyl-*p*-aminobenzoate** (*Fr. Cx.*). *Prop. Names.* BUTESIN (*Abbott Laboratories, London*), SCUROFORME (*Pharmaceutical Specialities (May & Baker) Ltd., London*).  
 $C_6H_4NH_2 \cdot COOC_4H_9 = 193.2$ .

Butyl-*p*-aminobenzoate is a white, crystalline, odourless and tasteless powder. M.p. 56°.

Almost *insoluble* in water; soluble in dilute acids, alcohol, chloroform, ether and fixed oils.

It is used as a local anæsthetic where prolonged and rapid anæsthesia is required, and is applied either as a powder or in the form of suppositories, ointment, or in alcoholic or oily solution.

[P1] **Butesin Picrate** (*Abbott Laboratories, London*). A compound of butyl-*p*-aminobenzoate and trinitrophenol, supplied in the form of a dusting powder 5%, as an ointment 1%, and as an eye ointment 1%. An analgesic-antiseptic for burns, scalds, ulcers, abrasions, etc.

Four cases of eruption following the use of Butesin Picrate ointment.—M. B. Sulzberger and F. Wise, *Arch. Derm. Syph.*, 1933, 461.

[P1] **Orthocaina** (B.P., *P. Helv. V*). *Syn. and Prop. Name.* AMINO-BENZ, ORTHOFORM (*Bayer Products, London*), METHYL *m*-AMINO-*p*-HYDROXYBENZOATE.

$\text{HO} \cdot \text{C}_6\text{H}_3(\text{NH}_2)\text{CO}_2 \cdot \text{CH}_3$  [ $\text{HO} : \text{NH}_2 : \text{CO}_2 \cdot \text{CH}_3 = 4 : 3 : 1$ ] = 167.1.

*Dose.*— $1\frac{1}{2}$  to 3 grains (0.1 to 0.2 g.) for stomach ulceration. *P. Helv. V* has max. single dose 15 grains; max. in 24 hours 45 grains. (The Council on Pharmacy and Chemistry of the A.M.A. does not approve of its internal use.)

A white crystalline powder, possessing local analgesic and anti-septic properties.

**Soluble** 1 in 7 of alcohol 90%, 1 in 50 of ether; readily soluble in sodium hydroxide solution; sparingly soluble in water.

The [P1] **Hydrochloride**,  $\text{HO} \cdot \text{C}_6\text{H}_3(\text{NH}_2)\text{CO}_2 \cdot \text{CH}_3 \cdot \text{HCl} = 203.5$ , is soluble about 1 in 9 of water, giving a strongly acid solution. The action of the base is more prolonged.

A 10% aqueous solution of the hydrochloride, or 10 to 20% with lanolin or paraffin ointment, or collodion solution of pure orthocaine, or this as a dusting powder, may be employed to alleviate pain in sores or burns, but has little action unless the surface is broken.

Has relieved whooping-cough and laryngeal tuberculosis by insufflation.

Eruption following application of 10% orthocaine ointment to septic ulcers of the foot.—P. C. P. Ingram, *Brit. J. Dermat.*, 1933, 526.

[P1-S1] **Phenacainæ Hydrochloridum** (U.S.P. XI). *Syn. and Prop. Name.* PHENETIDYLPHENACETIN HYDROCHLORIDE, HOLOCAIN HYDROCHLORIDE (*Bayer Products, London*).

$\text{CH}_3\text{C} \leq \begin{matrix} \text{N} \cdot \text{C}_6\text{H}_4 \cdot \text{OC}_2\text{H}_5 \\ \text{NH} \cdot \text{C}_6\text{H}_4 \cdot \text{OC}_2\text{H}_5 \end{matrix}$ ,  $\text{HCl} \cdot 2\text{H}_2\text{O} = 352.7$ .

The hydrochloride of ethenyl-*p*-diethoxydiphenylamidine in small colourless shining crystals.

**Soluble** 1 in 55 of water. **Incompatible** with alkalis.

As an anæsthetic in ophthalmology, 2 to 5 eye drops of 1% solution. It is not adapted for hypodermic use.

[P1-S1] **Guttæ Holocainæ** (R.L.O.H.). Holocain hydrochloride 4 gr. to 1 oz. of sterilised water.

[P1-S1] **Procainæ Hydrochloridum** (B.P., U.S.P. XI, *P. Helv. V*, *P. Dan.*, *P. Jap. V*).  $\text{NH}_2 \cdot \text{C}_6\text{H}_4 \cdot \text{CO}_2 \cdot \text{C}_2\text{H}_4\text{N}(\text{C}_2\text{H}_5)_2 \cdot \text{HCl} = 272.6$ . *Syn. and Prop. Names.* ETHOCAINE HYDROCHLORIDE (*F.E. VIII*), *p*-AMINO-BENZOYLDIETHYLAMINOETHANOL HYDROCHLORIDE (*Fr. Cx.*, *P. Ital. V*, *P. Argent. II*, *P.G. VI*, *P. Ned. V*, *P. Svec. X*, *P. Belg. IV*), ALLOCAINE, SYNCAINE, ÆTHOCAINE (*Nederlandsche Cocainefabriek, Amsterdam; Greef, London*), KEROCAIN (*Kerfoot, Bardsley*), NEOCAINE (*Corbière, Paris; Anglo-French Drug Co., London*), NOVOCAIN (*Bayer Products, London; Saccharin Corporation, London*), PLANOCAINE (*Pharmaceutical Specialities (May & Baker) Ltd., London*), SEVICAINE (*Glaxo Laboratories, London*).

*Dose.*— $\frac{1}{2}$  to 2 grains (0.03 to 0.12 g.) subcutaneously, up to 15 grains (1 g.); by intrathecal injection, up to  $2\frac{1}{2}$  grains (0.15 g.).

*Fr. Cx.* has max. single dose *per os* 0.1 g., max. during 24 hours 0.25 g.

A colourless crystalline salt melting at 154° to 156°. The aqueous solution is neutral to litmus.

**Soluble** 1 in 1 of water, 1 in 8 of alcohol 90%, 1 in 30 of dehydrated alcohol.

**Incompatible** with alkalis, tannin, calomel, potassium dichromate, potassium permanganate and silver salts. With the latter use procaine nitrate (3% solution).

**Sterilisation.** Acid solutions of procaine hydrochloride (pH 6 or less) are stable at normal temperatures, but on heating they become hydrolysed and the hydrochloric acid liberated catalyses the decomposition of the free procaine base into *p*-aminobenzoic acid and diethylaminoethanol. Hence, the minimum amount of heating in the process of sterilisation compatible with the production of a sterile solution is desirable. For this reason many workers deem Tyndallisation, as recommended by the B.P. to be unsuitable. A. E. Marston and J. P. Allchin (*Pharm. J.*, ii/1938, 603) found that solutions of 1% or over were germicidal to the commonly occurring air-borne organisms, and accordingly they state that sterile solutions of procaine hydrochloride of these strengths may be prepared by using an aseptic technique and heating to 60° for one hour only.

The decomposition of solutions on storage or heating, and its estimation.—F. Hartley, *Pharm. J.*, i/1938, 461.

**Alkaline solutions** are advocated on the grounds that they cause less pain both on injection and after, result in less tissue damage, thus leading to a more rapid recovery, and are more active. Tablets containing sodium bicarbonate or solutions buffered at about pH 8.0 with sodium phosphate have been recommended.

No alkaline solution of procaine hydrochloride may safely be sterilised by heating, since it either becomes acid or marked decomposition occurs. Neither may it be stored for more than six hours at room temperature. A method is described for the dispensing of dry ampoules suitable for the preparation of alkaline, sterile, isotonic and buffered solutions, and a report is given on the purity and the differences of commercial brands of procaine hydrochloride at present on the market.—K. Bullock, *Quart. J. Pharm.*, 1938, 407.

The use of distilled water in the preparation of Novocain solution must be condemned, because such a solution is markedly hypotonic. A 1% solution of Novocain in distilled water will hæmolyse red cells and rupture connective tissue and fat cells, resulting, in some cases, in enough tissue necrosis to cause breakdown of a perfectly aseptic wound. To obtain a practically isotonic solution, normal salt solution should be used to prepare Novocain solutions for infiltration purposes. Such solutions in saline are acid in reaction, but are promptly buffered in the subcutaneous tissues by the ample amounts of carbonates and phosphates in the tissues, which allow the Novocain base to exert its action. For the injection of nerve trunks or roots, however, a buffer solution such as Hartmann's solution is recommended as a solvent, and for spinal anaesthesia the best solvent is the patient's own spinal fluid. If Novocain solutions require to be autoclaved this should be done not more than 15 or 20 minutes before use, since oxidation of the Novocain occurs after this.—S. Gilman, *New Engl. J. Med.*, 1938, 841.

From a study of the evidence both for and against the use of alkalised or buffered solutions, there would appear to be no particular advantage of the most complex formula over the simplest freshly prepared procaine hydrochloride solution.—H. T. Roper-Hall, *Dental Gazette*, Oct. 1939, 90.

**Uses.** A powerful local anaesthetic, but its effect is very transient

unless adrenaline is added. It is much less toxic than cocaine and most other cocaine substitutes, and is well tolerated by the tissues. It is not satisfactory for surface anæsthesia, since it has little power of penetration. 0.25 to 2% solutions are employed for hypodermic use; care must be taken to avoid injection into a vein.

**Infiltration anæsthesia** (injection of the drug directly into the tissues to be operated on) has been practised, using 200 ml. of 0.5% solution in normal saline—a maximum dose. This is sufficient to anæsthetise the area for most operations. 50 to 75 ml. is enough for a moderate size elbow; 150 ml. for a knee. Solution tablets of procaine hydrochloride and adrenaline are available in various strengths.

**ACUTE STRAINS.** Immediate relief from pain, cessation of swelling and restoration of almost complete mobility of the joint follow the use of procaine infiltration (Leriche's method). This consists in infiltrating the periarticular tissues of the injured joint with a 2% solution of procaine (*without* adrenaline); in ankle sprains 10 to 15 ml. will suffice. Some hours later the pain returns, taking from 4 to 7 hours to pass off. In some cases it may be necessary to repeat the injection on the following day. As the "after-pain" is often very great, the treatment should be confined to severe or moderately severe sprains. Injection of physiological saline solution is stated to relieve the pain, which is thought to be due to the procaine itself. The average period of incapacity is reduced from 10 to 12 days to 2 to 3 days. The treatment also gives dramatic and lasting cure of minor complaints such as stiff neck, fibrositis, lumbago and vague muscular pains.—E. J. Moynahan, *Brit. med. J.*, i/1939, 671.

Successful results in 100 cases of minor fracture.—H. Cullumbine, *Lancet*, ii/1939, 552.

**MUSCULAR RHEUMATISM.** A method of treatment which secures not only immediate relief from pain, but prompt restoration of function in muscular rheumatism (e.g., stiff neck, lumbago, "pseudo-sciatica") consists in giving local injections of Novutox (or a 2% mixture of procaine and adrenaline). The injection is best given one-eighth of an inch beneath the surface of the fascia covering the affected muscle, the needle being inserted obliquely through the skin and the fascia then being felt for with the point. Through a single skin puncture, inject amounts of 0.5 ml. in each of 3 or 4 directions through separate punctures in the fascia. The patient should be warned that the injection is painful, and should also be warned of the tremor following the administration of adrenaline. After an hour's rest the patient should get up and move about. Stiffness is usually felt in the affected part for several days.—M. Button, *Brit. med. J.*, ii/1940, 183.

**Intrasacral extradural anæsthesia** for operations on hæmorrhoids, fistulæ, and other conditions in and about the anus. 20 ml. of 2% solution to which 5 drops of a 1 in 1000 adrenaline solution is added—the amount of procaine hydrochloride thus exceeds 6 gr. 15 gr. have been used in a local or regional anæsthesia, and even 35 gr. have been used.

Local anæsthesia in operations on the anal region has been effected by injection of solution consisting of procaine hydrochloride 2%, adrenaline (1 : 1000) 1% and phenazone 1%. An average injection of 2 oz. is preceded by hypodermic injection of morphine  $\frac{1}{4}$  gr. and hyoscine hydrobromide  $\frac{1}{100}$  gr.

**Regional anæsthesia** is a form of local anæsthesia by which the sensory nerve paths are blocked by injection of the anæsthetic into, or round, a nerve trunk, using a stronger solution than that for local infiltration. A small quantity is introduced round the nerve trunks which supply the parts to be operated on, at some part of their course which is anatomically accessible. This form

of anaesthesia has been effected with a solution of procaine hydrochloride 2, sodium chloride 0.5, distilled water 100. Five drops of a 1 in 10,000 solution of adrenaline are added to each 20 ml. of solution immediately before use.

**Methods described.** The multiplicity of punctures necessary, Novocain intolerance, and the psychic factor are disadvantages, but the technique is regarded as a life-saving measure in the surgery of the old and feeble, and those with cardiac, renal, or pulmonary disease, or diabetes.—Stanford Cade, *Lancet*, i/1925, 856.

**HERPES ZOSTER.** Twenty-two patients suffering from herpes zoster were treated by injections of a 0.5% procaine solution (without adrenaline) into the intervertebral and prevertebral ganglia, 8 ml. being as a rule used for each segment. Except in two patients the pain ceased and the vesicles dried within 24 to 48 hours. Two patients suffering from trigeminal zoster had their Gasserian ganglia injected with 1 and 2 ml. of this solution and in 48 hours the symptoms disappeared. Perfect asepsis is of the utmost importance, and the treatment should be abandoned if the only way of reaching the ganglion is through an area of infected vesicles—one should probably inject directly into the ganglion. Full segmentary anaesthesia results within 15 minutes of injection.—S. Rosenak, *Lancet*, ii/1938, 1056.

**TRIGEMINAL NEURALGIA.** The following technique gives good results. A small bleb of skin is first anaesthetised with Novocain and then a needle is gradually introduced towards the foramen ovale and Proctocaine 1 ml. injected drop by drop. The patient has an immediate anaesthesia of the affected side and the pain has been relieved. The relief in some cases is lasting, but in others re-injections are required at long intervals. There are no untoward results.—G. Slot, *Lancet*, ii/1938, 1329.

**Spinal anaesthesia** with procaine hydrochloride should be reserved for adults, and should not be used in the tuberculous, the syphilitic, or in nervous cases. Specially suitable for operations below the umbilicus. (*See also Amylocaine Hydrochloride*, p. 426.)

Barker's method of Stovaine-Glucose is not used so much now. Procaine hydrochloride is the least toxic of known local anaesthetics. Raising blood pressure by ephedrine injection simultaneously leads to rapid absorption and diminishes the anaesthetic effect. High spinal anaesthesia has many advantages (using 1 to 1.2 ml. of 10% procaine hydrochloride), and is safe if careful technique followed.—C. A. Pannett, *Lancet*, i/1929, 271, 291; *see also* W. Howard Jones, *Lancet*, i/1929, 362, and reply, *ibid.*, 416.

Deaths under spinal anaesthesia.—*J. Amer. med. Ass.*, ii/1930, 234; *Lancet*, ii/1930, 650.

In a series of 812 cases (inhalation anaesthesia 474, spinal anaesthesia 338) post-operative complications were 4.29 times more frequent after spinal than after inhalation anaesthesia, in spite of the fact that more "bad risk" patients were operated on under the latter.—A. L. Brown and M. W. Debenham, *J. Amer. med. Ass.*, ii/1932, 210.

As remedial measures for the circulatory depression of spinal anaesthesia are recommended: the raising of the lower part of the body, but not the lowering of the head; the inhalation of oxygen, and the inhalation of dilute ammonia. The injection of ephedrine or adrenaline is not recommended.—C. A. Pannett, *Lancet*, ii/1933, 169.

Headache following spinal anaesthesia, usually caused by seepage of spinal fluid from the dural wound, is minimised by using a fine needle (24-gauge), making a single puncture, and avoiding elevating the head for 24 hours. Merely using a fine needle so nearly abolishes headache that patients can comfortably become ambulatory within 24 hours.—A. W. Squires, *New Engl. J. Med.*, ii/1939, 898.

**Splanchnic analgesia** with procaine hydrochloride. Advantages are perfect relaxation of the abdominal wall with less shock and fatigue to patient. Disadvantages are the extra 15 minutes' time to anaesthetise patient, and in some cases post-operative

headache and backache. Operations may be performed which would not be attempted under general anæsthesia alone.

**UPPER ABDOMINAL SURGERY.** Braun's technique modified. The vertebral column between aorta and inferior vena cava is felt just above the pancreas with the left index finger through the lesser omentum. The finger is kept close to the right side of the aorta and the narrow tubular guide of the long fine needle passed along its dorsum down to the vertebra and kept there by the middle finger. The needle is then passed down the guide as far as the bone, aspiration performed to prove the point of the needle not to be in a blood vessel, and 30 ml. of 1% procaine hydrochloride solution containing 20 drops of 1 in 1000 adrenaline per 100 ml. injected. The viscera fall back into the abdomen and render it easy to inject a further 10 ml. of the solution to the left of the aorta behind the œsophagus.

The most commonly used local anæsthetic in abdominal surgery is procaine hydrochloride in  $\frac{1}{2}$  to 1% solution, with adrenaline. 1 g. procaine hydrochloride in  $\frac{1}{2}$ % solution can be used without injury. In cachectic and anæmic patients  $\frac{1}{2}$ % efficient (up to 500 ml.). In aged patients with arteriosclerosis add pituitary (posterior lobe) extract instead of adrenaline.

#### Choice of Methods of Anæsthesia:—

**ANTERIOR SPLANCHNIC** for radical operation after exploratory laparotomy.

**PARAVERTEBRAL**, in resections of large intestine to mobilise the fixed colon; for the resection.

*Mesenteric anæsthesia added.*

**PARASACRAL** sufficient for operations on rectum and perineum.

**EPIDURAL (SACRAL)** sufficient for pelvic operations.

**SPINAL** anæsthesia now little used in Germany owing to danger of fall of blood pressure and danger to respiratory centre.

*Combined parasacral safer and efficient for longer time.*

Prof. H. Finsterer, *Brit. med. J.*, ii/1932, 400.

[P1] **Injectio Procainæ et Adrenalinæ.** The Committee on Pharmacy and Pharmacognosy of the Pharmacopœia Commission (*Report 13*) have recommended the inclusion in the B.P. of procaine and adrenaline injection containing procaine hydrochloride 2%, sodium chloride 0.5%, *p*-chlor-*m*-cresol 0.1%, solution of adrenaline hydrochloride 2%, sodium metabisulphite 0.1%, in sterilised water.

[P1] **Injectio Procainæ et Adrenalinæ (R.L.O.H.).** *Syn.* INJECTIO NOVOCAINÆ ET ADRENALINI.

Procaine hydrochloride 8 or 16 gr., solution of adrenaline hydrochloride 24 m., sterilised water to 1 oz. (approx. 2 or 4%). *Dose.*—Up to 1 drachm of the 2%. In eye work may be employed, e.g., for excision of the lachrymal sac, and for other minor operations.

[P1] **Solutio Novocainæ Composita (St. T. H.).** *Syn.* DUNHILL'S SOLUTION. Novocain 3 gr., solution of adrenaline hydrochloride  $7\frac{1}{2}$  m., sodium chloride 14 gr., water to  $3\frac{1}{2}$  oz.

[P1] **Solutum Adrenalinæ Compositum (Fr. Cx.).** Procaine hydrochloride 2 g., solution of adrenaline 5 g., sodium sulphite 0.1 g., normal saline to 100 g. It is sterilised by Tyndallisation.

[P1] **Arecan (Evans, Sons, Lescher & Webb, Liverpool).** Solutions of procaine hydrochloride with adrenaline in various strengths.

[P1] **Asensitine (Duncan, Flockhart, Edinburgh).** A solution of 0.5% procaine, 2% eucaine and adrenaline 1 in 30,000 for local anæsthesia in dental operations. *Dose.*—1 to 2 ml. in divided doses.

[P1-81] **Duracaine (Pharmaceutical Specialities (May & Baker) Ltd., London).** Solution of Planocaine in 15% alcohol with gum acacia for intraspinal anæsthesia. Issued as (1) light solution—s.g. 1.002, ampoules of 3 ml.; (2) heavy solution—s.g. 1.028, ampoules of 3.5 ml.

[D-P1-81] **Epicaine (Burroughs, Wellcome, London).** Solution of Epinephrine 0.0003 g., and cocaine hydrochloride 0.02 g., per ml.

[P1] **Neotonocain** (*Richter, London*). Procaine hydrochloride and adrenaline in various strengths.

**Novocain-Cobefrin** (*Bayer Products, London*). A combination of procaine hydrochloride and Cobefrin, issued in [P1·S1] tablets and [P1] solutions of various strengths for local anaesthesia. Cobefrin is *o*-dioxypheylpropanolamine, a synthetic vasoconstrictor which dissolves readily in water, and exerts the vasoconstrictor action of adrenaline without its disturbing deleterious action on the circulation.

[P1] **Novutox** (*Pharmaceutical Mfg. Co., Cheltenham*). Procaine with isooctyl-hydrocupreine hydrochloride. A self-sterilising solution of procaine.

[P1] **Parsetic** (*Parke, Davis, London*). Procaine hydrochloride 2·25%, adrenaline chloride 1 : 30,000.

[P1·S1] **Spinocain** (*Bayer Products, London*). Each 2 ml. ampoule contains 0·2 g. of Novocain, 2·2 mg. of strychnine sulphate, and 14½% of alcohol in normal saline. It also contains gliadin or amyloprolamin.

The amount stated is mixed with more or less cerebrospinal fluid as required, and after injection the table is tilted to direct it to any region desired. In the circumstances of a modern operation a large fall of blood pressure is not greatly to be feared. Jonnesco gave up strychnine after 15 years' trial. A similar solution to Spinocain, but without the strychnine, gave equally good results. No evidence to show that addition of dextrin is not as good as gliadin.—E. Falkner Hill, *Lancet*, i/1930, 124.

Thought to be an improvement on Stovaine, the use of which was often followed by collapse.—C. L. Granville Chapman, *Brit. med. J.*, i/1930, 799; see also R. A. Grant, *Brit. med. J.*, i/1930, 1090.

Spinal anaesthesia with Spinocain, using Ephedrine-Novocain first. 250 cases.—A. Wilfred Adams, *Brit. med. J.*, i/1931, 785. Death under.—A. Wilfred Adams, *ibid.*, i/1931, 869.

[P1·S1] **Procaine Borate**. *Prop. Name.* BOROCAINE (*British Drug Houses, London*).

$2(C_{13}H_{20}O_2N_2) \cdot 5B_2O_3 \cdot 4H_2O$ . Available as the substance and in tablets with or without adrenaline. Although a salt of procaine, it is stated to be more active but less toxic than procaine hydrochloride. The difference in properties is due to the fact that procaine borate, being the salt of a weak acid, in solution yields free alkaloidal base by hydrolysis. It is employed by injection and as a surface anaesthetic in minor surgical operations, especially in dental practice.

For ophthalmic and dental use, for operations on and examination of the urethra and bladder, and for surface anaesthesia in general, 2% solutions are used, and for operations on the nose and throat 5% solutions. (Beta-Borocaine, *v. antea*, is stated to be a better surface anaesthetic.) For infiltration anaesthesia solutions of 0·5 to 1% are employed, and for regional anaesthesia from 1 to 2%.

An account of the borates of some anaesthetic bases ("borocaines").—A. J. Copeland and H. E. F. Notton, *Brit. med. J.*, ii/1925, 547.

A 2% solution of Borocaine is an improvement on a 0·5% solution of cocaine, in urethral anaesthesia, and a 1% solution of the former gives better anaesthesia than a 0·5% solution of cocaine, but a 0·5% solution of Borocaine has no advantage over a 0·3% solution of cocaine. Beta-eucaine borate in 0·5% solution is a perfect urethral anaesthetic and the relaxation is perfect. In ½% its action is equal to ¼% cocaine hydrochloride, but ¼% is not so good as ½% cocaine.—R. Coyte, *Brit. med. J.*, i/1926, 85.

**OPHTHALMOLOGY.** Borocaine greatly inferior to cocaine as regards surface anaesthetic effect. Cocaine is perfectly reliable, whereas the effect of Borocaine is variable.—T. H. Butler and R. U. Gillan, *Brit. med. J.*, i/1926, 84.

[P1-81] **Butyn** (*Abbott Laboratories, London*). *p*-Aminobenzoyl- $\gamma$ -di-*n*-butyl-aminopropanol sulphate.

$[\text{NH}_2 \cdot \text{C}_6\text{H}_4 \cdot \text{COO}(\text{CH}_2)_3\text{N}(\text{C}_4\text{H}_9)_2]_2\text{H}_2\text{SO}_4 = 710.6$ .

A white amorphous powder, freely *soluble* in water, less soluble in alcohol, acetone and chloroform; insoluble in ether.

*Incompatible* with chlorides and salicylates.

**Uses.** A local anæsthetic especially recommended for surface anæsthesia of the eye, nose and throat. For surface anæsthesia of the eye a 2% solution is employed; a few drops of this suffice for the removal of a foreign body. It does not dilate the pupil or affect accommodation. The 2% solution is also suitable for general application to the tonsils and to the mucosa of the throat, mouth and nose. For subcutaneous injection and for infiltration anæsthesia in tonsillectomy from 0.1 to 0.25% solutions are used.

Contraindicated where there is a solution of continuity in the mucous membrane, either through trauma or ulceration, as this allows too rapid absorption of the drug.—W. R. Jamieson, *J. Amer. med. Ass.*, i/1929, 1519.

[P1-81] **Butyn Oral Obtundent** (*Abbott Laboratories, London*). Butyn sulphate 10%, alcohol (95%) 10%, aqueous solvent 80%. For topical application as a local anæsthetic in dental work.

[P1-81] **Butethanol**. *Syn. and Prop. Names.* PANTOCAINE, TETRA-CAINE, ANETHAINE (*Glaxo Laboratories, London*), DECICAIN (*Bayer Products, London*), PONTOCAINE HYDROCHLORIDE (*Winthrop, New York*).

$\text{C}_4\text{H}_9 \cdot \text{NH} \cdot \text{C}_6\text{H}_4 \cdot \text{COO} \cdot \text{C}_2\text{H}_4 \cdot \text{N}(\text{CH}_3)_2 \cdot \text{HCl} = 300.68$ .

Butethanol is *p*-butylaminobenzoyldimethylaminoethanol hydrochloride, and occurs as a white crystalline powder melting at 148° to 150°.

**Soluble** 1 in 7 of water; also soluble in alcohol; insoluble in ether.

**Uses.** A local anæsthetic of the procaine series, used in 2% solution for surface anæsthesia and in 0.5 to 1% solution for spinal anæsthesia. For infiltration anæsthesia a 1 in 1000 solution in normal saline with adrenaline is employed; for ophthalmology a 0.5% solution has been employed, but it is reported to cause irritation and turbidity of the cornea. Butethanol is claimed to be fifteen times as active as procaine and ten times as active as cocaine, but is more toxic. It should be combined with adrenaline to minimise toxic reactions.

[P1-81] **Decicain L, Dry Substance** is issued in ampoules containing 10 mg. of dry Decicain, together with ampoules containing 2 ml. of Racedrin (racemic ephedrine), for spinal anæsthesia.

**Decomposition on Sterilisation.** The decomposition of Decicain solutions increases with temperature and hydrogen ion concentration. A solution in N/1000 hydrochloric acid is very stable.—A. Rae, *Pharm. J.*, ii/1938, 24.

**Impletol** (*Bayer Products, London*). A molecular compound of procaine hydrochloride and caffeine.

**Dose.**—2 ml. subcutaneously or intramuscularly. In migraine, dysmenorrhœa and pain due to vasomotor disturbances.

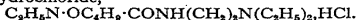
[P1-81] **Metycaine** (*Lilly, London*). Hydrochloride of  $\gamma$ -(2-methyl piperidino)-propyl benzoate. A local anæsthetic producing prompt anæsthesia either by infiltration or by application to mucous membranes.



Dosage for mucous membranes: eye 2%; nose and throat 2 to 10%; urethra 1 to 4%. It is supplied either in powder, tablets, solution or ampoules.

[P1-S1] **Panthesine** (*Sandoz, London*). N-Diethyl-leucinol ester of *p*-amino-benzoic acid. A local anæsthetic stated to have a surface anæsthetic action equal to that of cocaine with only one-third the toxicity. It may also be employed for infiltration and spinal anæsthesia. Issued in solution and ampoules and as powder. [P1] **Panthesine Balm** containing 5% of Panthesine is indicated in rheumatism, gout, neuralgia, etc.

[P1-S1] **Percaïne** (*Ciba, Horsham*). (*Syn.* NUPERCAINE in U.S.A.). The hydrochloride of  $\alpha$ -butyloxycinchoninic acid diethylethylene-diamide or 2-butyloxyquinolinecarboxylic acid-4-diethylethylene-diamide hydrochloride,



It is supplied as base or hydrochloride and in 2% solution (for surface anæsthesia), also in solutions of various strengths for spinal anæsthesia, and in solution and tablets with adrenaline.

**Dose.**—For infiltration anæsthesia solutions of from 1 in 2000 to 1 in 1000 with addition of 0.1 ml. of adrenaline hydrochloride solution (1 in 1000) to 100 ml. Not more than 100 ml. of 1 in 1000 solution should be injected. For spinal anæsthesia from 7.5 to 10 mg. in 1 in 200 solution. For sacral anæsthesia 25 to 35 ml. of 1 in 1000 solution. Solutions should be prepared with distilled water, and alkali-free glass used.

Colourless crystals, m.p. 97°. Readily *soluble* in water, alcohol, chloroform and acetone, but insoluble in ether and oils. Solutions are made in normal saline, giving neutral solutions.

**Toxic Effects.** The symptoms of poisoning are clonic convulsions, motor excitement, acceleration of respiration, and ultimate paralysis. Deaths have followed its use for spinal anæsthesia.

Fatal syncope following Percaïne in operation for a large ovarian cyst. The prone position is an error. It should be remembered that the gravid uterus is a similar contraindication.—W. Howard Jones, *Lancet*, ii/1930, 550.

Used as a local anæsthetic in abdominal surgery, caused necrosis of the tissues. Prof. Finsterer (Vienna) reported two deaths within 24 hours following its use.—*Brit. med. J.*, ii/1932, 400.

Two deaths following lumbar anæsthesia with 2 ml. and 10 ml. of 0.4% solution.—*Per Brit. med. J.*, ii/1933, 95.

Death of a woman of 69 following the subcutaneous injection of 2% Percaïne solution. At the inquest the medical practitioner said that while he had ordered procaine from the chemist he had employed the 2% Percaïne solution mistakenly sent, since he thought that the reference to this strength solution in the makers' literature for use in "surface anæsthesia" meant that it was suitable for use by subcutaneous injection.—*Pharm. J.*, ii/1939, 370.

**Uses.** A local anæsthetic for infiltration and spinal anæsthesia, acting like cocaine when applied to mucous surfaces and like cocaine or procaine when injected, the action being relatively prolonged. Its toxicity is three times that of cocaine and about twenty-five times that of procaine when injected subcutaneously, hence it should not be employed by this route.

It is potent in such high dilution that the content adds next to nothing to the sp. gr. of the vehicle. For thoracic nerve root blocks, solutions 1 in 2000 to 1 in 1000 according to duration of analgesia needed. 7½ to 10 mg. said to be more effective than 150 mg. of procaine hydrochloride.—W. Howard Jones *Lancet*, i/1930, 573.

Mucous membranes, especially of the nose, anæsthetised with 1 and 2% solutions, with addition to each 50 ml. of  $\frac{1}{2}$  ml. of adrenaline solution, for partial resections of turbinates, removal of polypi, ethmoidal curettages, and intranasal drainage of maxillary antrum.—O. Popper, *Brit. med. J.*, i/1930, 669.

Has far greater toxicity and no great advantage over Novocain-adrenaline for infiltration anesthesia but promising for mucous membranes.—M. C. G. Israels and A. D. Macdonald, *Brit. med. J.*, ii/1931, 986.

The least toxic of the spinal analgesics. Effect on blood pressure considerably less; the effect lasts from 1 to 3 hours and the patient is free from pain for from 6 to 12 hours after the operation, while a smaller number of headaches occur than with Stovaine, etc. High abdominal anesthesia can be produced with maximum of safety, and the same solution used to infiltrate the skin before introducing the intrathecal needle. The dilute solution (20 ml. of a 1 in 1500 solution) is more often used, but the stronger (2.3 ml. of a 1 in 200) is useful for operations on the perineum, etc., using doses of 0.6 ml. up to 2.3 ml., and operations such as removal of piles, cystoscopy and prostatectomy may be done with this strong solution. Premedication with Omnopon and scopolamine is given one hour before operation. Howard Jones' technique described, as used in 1200 cases. Injection in the upright sitting position the technique of choice for pregnancy, patients with large abdominal tumours, and similar cases.—R. Jarman, *Brit. med. J.*, i/1934, 797.

Prof. Sebrechts, of Bruges, from an experience of 35,000 cases, considers spinal anesthesia with Percaine the method of choice for abdominal surgery, using 15 to 20 ml. of the 1 in 1500 solution in fractional doses of 5 ml. at 5-minute intervals. Individuals vary in their reaction, ignorance of which probably accounts for most of the former failures and disasters. An injection of  $\frac{1}{4}$  gr. of morphine and  $\frac{1}{16}$  gr. of scopolamine an hour before operation helps in estimation of patient's response, the sensitive being deeply narcotised; the normal, somnolent; and the resistant unaffected.—*Brit. J. Anæsth.*, Oct., 1934, 4.

*For details of use of Percaine in oil in the treatment of pruritus ani and anal fissure, see p. 430.*

[P1-81] **Unguentum Sedativus (St. T.H.)**. Percaine (base) 2, liquefied phenol 1.25, solution of hamamelis 10, simple ointment 86.75.

[P1-81] **Percainol (Ciba, Horsham)**. Ointment containing 1% of Percaine with solution of hamamelis and aluminium formate. Anti-pruritic and analgesic application for skin diseases.

[P1-81] **P.B.A. (Allen & Hanburys, London)**. An oily solution containing Percaine 0.5%, benzyl alcohol 10%, phenol 1%. Ampoules contain 5 ml. for subcutaneous injection in pruritus ani, anal fissure, etc.

[P1-81] **Phenolaine (Phenolaine Co., London)**. The preparation is stated to contain methyl, ethyl, benzoic and carboxyl groups and an amine group. It has been used in a large number of operations without trouble as regards bleeding or subsequent after-effects. It does not produce vasodilatation on subcutaneous or intramuscular injection.

*Dose*.—For general surgery, e.g., for hernia or appendicitis, use 2 drops of Phenolaine to each ounce of sterile water. Not more than 6 ounces of the dilution should be used at one time. For teeth extraction use 8 drops to 1 ounce of water. Amputations of the breast have been conducted with 12 drops in 6 ounces of water.

[P1-81] **Tutocain (Bayer Products, London)**. *Syn.* BUTAMIN.  
 $C_{14}H_{25}O_2N_2 \cdot HCl = 286.65$ .

Tutocain is *p*-aminobenzoyldimethylamino-1:2-dimethyl propanol hydrochloride. It is a light, ivory-coloured, odourless crystalline powder, with a faintly bitter taste. M.p.  $212^{\circ}$  to  $215^{\circ}$ .

*Soluble* about 1 in 4 of water and 1 in 40 of alcohol.

*Uses*. A local anæsthetic applicable for surface and infiltration anesthesia. It is about one-third as toxic as cocaine and from two to four times as toxic as procaine hydrochloride. For surface

anæsthesia, a 3 to 5% solution is used and for infiltration a 0.2% solution.

The most suitable strength for urethral work is  $\frac{1}{4}$  to  $\frac{1}{2}$ % with adrenaline.—*Per Prescriber*, Jan., 1927, 7.

Tutocaine more toxic than procaine hydrochloride, but quicker in action. 1 in 500 solution proved a reliable anæsthetic.—H. V. Molesworth, *Brit. med. J.*, i/1930, 13.

## CODEINA

*B.P.*, *U.S.P. XI*, *P. Ned. V*, *P. Ital. V*, *Fr. Cx.*, *P. Helv. V*,  
*P. Dan.*, *F.E. VIII*, *P. Belg. IV*.



[P1] "Alkaloids, the following; their salts, simple or complex:—Codeine."

[S1] "Alkaloids, the following; their salts, simple or complex:—Codeine except substances containing less than 1% of codeine."

Note.—Although codeine and its salts are controlled by the *Methylmorphine and Ethylmorphine Regulations*, 1933, these regulations do not affect any sale or distribution by an authorised seller of poisons in the course of any retail business (see page 1145).

Codeine and Dangerous Drugs Act, 1932.—It was argued at the 1925 Geneva Convention that codeine could be converted into drugs of addiction. Codeine being usually manufactured from morphine, it is open to a manufacturer, if codeine remains exempt from control, to buy codeine in the open market without the knowledge of the Government; he can then divert a corresponding amount of morphine into the illicit traffic and explain its disappearance by saying that he has converted it into the codeine. It was finally agreed that the restrictions should only relate to manufacture, export and wholesale trade.—*Brit. med. J. Supplement*, Mar. 5, 1932.

**Dose.**— $\frac{1}{4}$  to 1 grain (0.016 to 0.06 g.). *Fr. Cx.* has maximum single dose 0.08 g., maximum during 24 hours 0.3 g. *P. Helv. V* has  $1\frac{1}{2}$  and 5 grains respectively. *U.S.P. XI* average dose  $\frac{1}{2}$  grain.

An alkaloid from opium or manufactured from morphine, in colourless crystals, melting, after drying at 100°, at 155° to 156°. It is a methyl ether of morphine—monomethyl-morphine.

**Soluble** 1 in 120 of water, 1 in 2 of alcohol 90%, 1 in 13 of benzene, 1 in 20 of ether; also in chloroform and in excess of aqueous ammonia, but insoluble in excess of potash solution; very soluble in dilute acids.

**Antidotes.** Treat as for poisoning by morphine, see p. 697.

**Addiction.** Codeine has a relatively feeble euphoric action and the addict can get little satisfaction from the drug taken by the mouth, but large doses of codeine taken hypodermically (e.g., up to 50 gr. daily), or intravenously, can act as a morphine substitute for the addict. On the other hand, it is said that a normal individual, not familiar with the effects of morphine, who takes small daily doses of codeine, say,  $\frac{1}{4}$  or  $\frac{1}{2}$  gr. three times daily inevitably becomes a "codeinist" within two months.

While the question as to whether the administration of codeine results in genuine addiction cannot be answered in the negative, there are no sufficiently conclusive findings to justify an affirmative reply—only seven cases of primar

codeine addiction have been recorded in the literature. On the other hand the parenteral administration of codeine has brought about a new state of affairs, since it seems possible for a genuine primary codeine addiction to occur even in persons not previously addicted to drugs, though in order to create this addiction very large doses are necessary parenterally. The new vogue of codeine injections undoubtedly represents a social danger. At the same time there cannot be said to be any *general* social danger, and the evil can be put down by national legislation without any need to set in motion the elaborate machinery of international regulation. The medical practitioner should not allow himself to be deterred from prescribing codeine freely in the usual small therapeutic doses, and he is still as justified as ever in regarding codeine as a good remedy without any dangerous accessory effects, though in the case of persons who have formerly been addicted to morphine or other drugs, or persons who are constitutionally predisposed to addiction, the doctor should no doubt avoid codeine as far as possible.—P. Wolff, *Bull. Hlth Org., L.O.N.*, 1938, 546.

Codeine addiction seems to have constituted a real problem in Canada in recent years. It is stated that Canada leads the world in the *per caput* consumption of codeine. The habit may arise without any relationship to previous addiction to morphine or heroin.—E. W. Adams, *Bull. Hyg.*, 1937, 241.

Withdrawal symptoms appear, as a rule, much later than in cases of morphinism. When the total dose of codeine sulphate varies from  $1\frac{1}{2}$  to 3 gr. daily, the symptoms of withdrawal are definitely felt on the fifth and sometimes even on the sixth day of abstinence. When Rossium is given, codeinists, as a rule, are freed from the craving very quickly.—I. Ostrofnislensky, *Med. Pr.*, ii/1936, 30.

**Uses.** Codeine is less narcotic, less constipating and less apt to induce a habit or tolerance than morphine. In moderate doses is hypnotic and in frequent small doses it allays cough in phthisis. For cough following catarrh  $\frac{1}{2}$  to 1 grain gives relief. In diabetes, beginning with  $\frac{1}{4}$  grain thrice daily, it lessens the amount of sugar in the urine. A useful sedative in chronic cystitis with enlarged prostate.

Codeine can be used instead of morphine in nearly every case except when the aim of treatment is to relieve pain; it is especially useful in chronic diarrhoea and should be used a good deal more than it is. Unless there is pain to be relieved, codeine, in an appropriate dose, is preferable to morphine for the purpose of producing rest in internal hæmorrhage.—R. H. Micks, *Practitioner*, i/1937, 532.

More than 75% of true common colds can be aborted in the early stages by taking  $\frac{1}{2}$  gr. each of codeine and papaverine five times daily for two days immediately the cold threatens.—F. Hutter, *Wien. klin. Wschr.*, i/1937, 376.

In the great majority of tuberculous patients requiring medication for cough relief, codeine, 10 mg. orally, is a sufficient dose.—L. F. Davenport, *J. Pharmacol.*, 1938, 64, 242.

**[P1-81] Capsulæ Codeinæ et Valerianæ Compositæ.**

*Dose.*—1 or more *p.d.* according to strength.

Codeine  $\frac{1}{2}$  to 1 gr., extract of valerian 2 gr., phenol 2 gr., extract of cascara  $1\frac{1}{2}$  gr. In glycosuria, codeine is valuable for treatment, the valerian is a nerve sedative and the phenol is an intestinal disinfectant.

**[P1-81] Capsulæ Codeinæ cum Extracto Cannabis.**

Codeine  $\frac{1}{2}$  gr., extract of cannabis  $\frac{1}{2}$  gr.

In neuralgia, 1 every 4 or 5 hours.

**[P1] Gelatinum Codeinæ (B.P.C.). Syn. CODEINE AND GLYCERIN JELLY.**

*Dose.*—1 drachm (4 g.). A lemon-flavoured preparation containing about 0.2% of codeine, equivalent to about  $\frac{1}{2}$  gr. in 1 drachm.

Useful in chronic laryngitis, phthisical cough, etc. Also in ulcer of the stomach.

**[P1] Pastilli Codeinæ (B.P.C.)** contain  $\frac{1}{2}$  gr. (0.008 g.).

**[P1-81] Pilula Codeinæ Composita.**

Codeine  $\frac{1}{2}$  gr. (increased to 2 gr. if necessary), extract of nux vomica  $\frac{1}{2}$  gr., extract of lettuce  $\frac{1}{2}$  gr. or more, mucilage *q.s.* to make one pill. To be taken 2 or 3 times a day, for diabetes.

**[P1] Sirop de Codéine (Fr. Cx.)** contains 0.2% *w/w* of codeine in 5% of alcohol 60% and "cold-prepared" simple syrup.

[P1-S1] **Codeinæ Hydrobromidum.**  $C_{18}H_{21}O_3N, HBr, 2H_2O = 416.1$ .

An anti-spasmodic similar in dose and use to the phosphate. For eye work has been advised to take the place of ethylmorphine—being said to cause less pain.

[P1-S1] **Codeinæ Hydrochloridum** (*P. Ned. V, P. Ital. V, P. Helv. V, P. Dan.*).  $C_{18}H_{21}O_3N, HCl, 2H_2O = 371.7$ .

*Dose.*— $\frac{1}{4}$  to 2 grains (0.016 to 0.12 g.). White crystalline powder, soluble 1 in 30 of water.

[P1-S1] **Codeinæ Phosphas** (*B.P., U.S.P. XI, P. Jap., Fr. Cx., P.G. VI, P. Helv. V, P. Dan., P. Ital. V, P. Belg. IV*).

$C_{18}H_{21}O_3N, H_3PO_4, H_2O = 415.2$ . *U.S.P. XI* has  $1\frac{1}{2} H_2O$ ; *P. Jap. V* has  $2 H_2O$ .

*Dose.*— $\frac{1}{4}$  to 1 grain (0.016 to 0.06 g.). *Fr. Cx.* has max. during 24 hours 6 grains approximately.

In granular snow-white crystals, containing 69% of anhydrous alkaloid. Is suitable for hypodermic injection, 1 grain in 15 minims (1 ml.).

**Soluble** 1 in 3.5 of water, 1 in 350 of alcohol 90%; sparingly soluble in ether and chloroform.

[P1] **Linctus Codeinæ** (*B.P.C.*).

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Contains codeine phosphate  $\frac{1}{4}$  gr. with citric acid, emulsion of chloroform, glycerin and mucilage of tragacanth to 1 drachm.

[P1-S1] *St. T. H.* has syrup of codeine phosphate 50% *v/v* in similar vehicle.

[P1] **Linct. Codein. Co.** (*N.I.F.*).

Syrup of codeine phosphate and syrup of tolu, equal parts.

[P1-S1] **Pilulæ Codeinæ et Belladonnæ** (*C.X.H.*).

Codeine phosphate  $\frac{1}{4}$  gr., dry extract of belladonna  $\frac{1}{4}$  gr., kaolin  $2\frac{1}{2}$  gr., hard soap to 4 gr.

A combination of two drugs with marked antispasmodic action and power to relieve pain originating in plain muscle. Designed for administration in painful colospasm. To be taken regularly over a period of weeks for full effect. —E. C. Warner, *Practitioner*, 1935, 831.

[P1] **Syrupus Codeinæ Phosphatis** (*B.P.C.*).

*Dose.*— $\frac{1}{2}$  to 2 drachms (2 to 8 ml.).

Codeine phosphate 0.5% in a solvent of distilled water and syrup. Contains about  $\frac{1}{4}$  gr. of codeine phosphate per drachm.

[P1] **Tab. Codein. Co.** (*N.I.F.*). Acetylsalicylic acid 4 gr., phenacetin 4 gr., codeine phosphate  $\frac{1}{4}$  gr.

[P1] **Codeoforme Botal Tablets** (*Bottu, Paris; Continental Laboratories, London*). A laryngeal sedative for all forms of cough. *Dose.*—1 to 5 tablets daily according to age and the nature of the cough. Each tablet is stated to be equivalent to codeine  $\frac{1}{16}$  gr., bromoform 4 m., tincture of aconite 1 m., tincture of belladonna 1 m., with terpene  $\frac{1}{8}$  gr. and sodium benzoate  $\frac{1}{4}$  gr.

[P1] **Vagocodaine** (*Richter, London*). Tablets contain aspirin 4 gr., phenacetin 4 gr., codeine  $\frac{1}{4}$  gr. *Dose.*—One tablet once or twice daily after meals. Antipyretic and analgesic.

[P1] **Veganin** (*Warner, London*). Acid acetylsalicyl. 32.68%, codeine 0.99%, phenacet. 32.68%, excipient ad 100. One tablet weighs 11.8 gr.

[P1-S1] **Codeinæ Sulphas** (*U.S.P. XI*).

$(C_{18}H_{21}O_3N)_2, H_2SO_4, 5H_2O = 786.5$ .

*Dose.*— $\frac{1}{4}$  to 1 grain (0.016 to 0.06 g.).

White crystals efflorescent in air; soluble 1 in 40 of water, slightly soluble in alcohol.

Given with advantage in sciatica, also in morphine habit, *q.v.*

**Apocodeinæ Hydrochloridum.**  $C_{15}H_{19}O_2N \cdot HCl = 317.6$ .

*Dose.*— $\frac{1}{16}$  gr. gradually increased to 1 grain (0.006 to 0.06 g.). 3 or 4 grains daily may safely be given. A greyish, hygroscopic powder consisting of the salt of the base or mixture of bases obtained by the action of zinc chloride on codeine. Soluble in water, less soluble in alcohol.

*Uses.* Is a sialogogue and sedative, and increases peristalsis. Is more expectorant than apomorphine and less emetic. Has been used in chronic bronchitis and other bronchial affections. Hypodermically 30 minims of 1% solution ( $= \frac{1}{4}$  gr.) may purge in half an hour or less, but may also prove emetic.

[D-P1-S1] **Dicodid** (*Knoll, London*). Dihydrocodeinone acid tartrate (for oral use) or hydrochloride (for subcutaneous injection). In white crystals soluble in water. Its activity is midway between that of morphine and codeine with specific influence on the cough centre. Tablets contain  $\frac{1}{3}$  gr. or  $\frac{1}{2}$  gr. Ampoules contain  $\frac{1}{2}$  gr.

*Dose.*—For cough and less severe pain  $\frac{1}{3}$  gr. orally, 2 or 3 times daily, increased if necessary. Subcutaneously, half to one ampoule. Should not be administered on an empty stomach.

[D-P1-S1] **Dilaudid** (*Knoll, London*). *Syn.* DIHYDROMORPHINONE HYDROCHLORIDE.  $C_{17}H_{19}O_3N \cdot HCl = 321.6$ .

*Dose.*— $\frac{1}{16}$  gr. *per os* or  $\frac{1}{32}$  gr. subcutaneously. This dose is effective for 4 to 6 weeks without increasing. Tablets are available containing 0.0025 g. of the hydrochloride. Also issued in ampoules containing 0.002 g. in 1 ml., and in combination with scopolamine hydrochloride 0.0003 g., and with atropine sulphate 0.0003 g.

*Soluble* in water and alcohol, insoluble in ether. The analgesic effect of  $\frac{1}{16}$  gr. of Dilaudid is equivalent to that of  $\frac{1}{8}$  gr. of morphine. It is not suitable for infants.

*Uses.* Dilaudid is a powerful analgesic allied to morphine, with a marked depressant action on the respiratory mechanism, and alarming symptoms of respiratory paralysis may occur even with therapeutic doses. It is more toxic than morphine, and is effective in smaller doses, and it is equally liable to give rise to addiction. Nausea, vomiting and constipation are less frequent than with morphine. It is especially indicated for the relief of all types of severe pain and to allay incessant cough without expectoration.

Used with beneficial effects in pleurisy, sciatica, facial neuralgia, angina pectoris, and acute arthritis, to replace morphine, but of no value when morphine addiction has developed. Unlike morphine, it is not necessary to increase the dose. It may cause transient nausea, giddiness, and confusion, but does not cause constipation or affect the appetite.—O. Leyton, *Lancet*, i/1932, 835.

[D-P1-S1] **Eukodal** (*Merck, Darmstadt; Savory & Moore, London*). *Syn.* DIHYDRO-HYDROXYCODEINONE HYDROCHLORIDE, EUCODAL.  $C_{18}H_{21}NO_4 \cdot HCl = 351.6$ .

*Dose.*— $\frac{1}{16}$  gr. (0.005 g.) *per os*, or  $\frac{1}{8}$  to  $\frac{1}{4}$  gr. (0.01 to 0.02 g.) subcutaneously.

White crystalline powder soluble in water. M.p. 270°.

Analgesic and hypnotic, used as a substitute for morphine; it is less toxic and shows less by-effects.

For preparations of Eukodal *exempt* [D] see p. 1142.

**Eukodal, Dicodid and Dilaudid.** Eukodal differs from Dilaudid and Dico- did in that it does not cause convulsions, and very large doses are needed to cause death. The toxicity of Dilaudid is much greater than Dico- did. The pharmacological actions of all of them are very similar to morphine, but they are much more toxic; smaller amounts of Dilaudid than morphine are needed to depress the respiratory centre. Eukodal has a much weaker action on the movements of the alimentary tract than the other two, and does not increase special reflexes, but it has a profound effect on respiration, as marked as that produced by either Dilaudid or morphine. There is no reason to think that any of these drugs are superior to morphine from a therapeutic point of view. —G. N. Myers, *Brit. med. J.*, i/1933, 981.

Pharmacological action of Dilaudid, Dico- did and Eukodal.—G. N. Myers, *Brit. med. J.*, ii/1933, 282.

**Paracodin** (Knoll, London). Dihydrocodeine. Tablets contain  $\frac{1}{4}$  grain. Dose.—1 to 3 tablets thrice daily. Also available in 1 ml. ampoules. Indications as for codeine. **Paracodin Syrup** contains 0.2% of Paracodin.

## COLCHICUM

[P1] "*Alkaloids, the following; their salts, simple or complex:—Colchicine.*"

[S1] "*Alkaloids, the following; their salts, simple or complex:—Colchicine except substances containing less than 0.5% of colchicine.*"

[P1] **Colchici Cormus** (B.P.).

Dose.—2 to 5 grains (0.12 to 0.3 g.) of the dried corm.

The corm of the meadow saffron, *Colchicum autumnale* (Lili- aceæ). Both fresh and dried corm are official, although the former is not used in making any preparations. The dried corm contains not less than 0.25% of colchicine.

**Toxic Action.** Colchicum affects the gastro-intestinal mem- brane. It may cause pains in the bowels, vomiting, diarrhœa, intense thirst, and violent burning in the throat, œsophagus and stomach.

**Antidotes.** Empty stomach by emetic, or by stomach tube using dilute tannic acid solution. Give repeated large doses of medicinal charcoal. Keep patient warm; give demulcent drinks freely. Dextrose may be administered intravenously, or saline infusion may be necessary. Atropine,  $\frac{1}{16}$  gr., and morphine,  $\frac{1}{4}$  gr., hypodermically to check diarrhœa. Strychnine,  $\frac{1}{8}$  gr., or caffeine sodium benzoate, 2 gr., hypodermically for collapse.

**Uses.** Has specific effect in gout, relieving pain and reducing inflammation in the acute attack, but has no prophylactic action. It may be given in pill with ipecacuanha and mercury, or as the tincture in mixtures. To abolish the vomiting and diarrhœa often produced, a small dose of atropine may be given with it. If any symptoms of gastric or intestinal irritation appear its use must be discontinued for a time.

Colchicum is probably the best and safest drug for all-round use to relieve pain during the acute attack of gout, and is best given in combination with purga- tives, as in the following mixture: tincture of colchicum 20 m., magnesium sulphate 30 gr., heavy magnesium carbonate 10 gr., peppermint water to 1 oz.; two ounces to be taken immediately and then one ounce every four hours.

Elderly persons need not be given more than 15 to 20 m. of the tincture as the initial dose. After 24 to 36 hours the dose of mixture should be reduced to half ounce and then omitted as soon as the acute stage has subsided.—Whittle.

**[P1-81] Extractum Colchici Aceticum (B.P.C.).**

*Dose.*— $\frac{1}{4}$  to 2 grains (0.016 to 0.12 g.).

An unstandardised soft extract prepared by evaporating the juice of the corm to which acetic acid has been added.

**[P1-81] Extractum Colchici Siccum (B.P.).**

*Dose.*— $\frac{1}{4}$  to 1 grain (0.016 to 0.06 g.).

The 60% alcohol extractive adjusted with lactose to contain 1% of colchicine. *Fr. Cx.* extracts seeds with 70% alcohol, not standardised. Max. single dose  $\frac{3}{4}$  grain, max. in 24 hours 3 grains approx. *P. Ital. V* extracts with alcohol 60% standardising to 2% of colchicine, *P. Belg. IV* and *F.E. VIII* use 70% with same standard.

**[P1] Liquor Antirheumaticus Compositus.**

*Dose.*—30 minims (2 ml.).

Colchicum wine 15, spirit of ether 5, camphor 2, compound tincture of lavender to 30.

**[P1] Pilulæ Colchici et Aloes (B.P.C.).**

*Dose.*—1 to 4 pills.

Contain  $\frac{1}{2}$  gr. each of dry extract of colchicum, dry extract of hyoscyamus and aloes.

**[P1] Pilulæ Colchici et Hydrargyri (B.P.C.).**

*Dose.*—1 to 3 pills.

Contain  $\frac{1}{2}$  gr. of dry extract of colchicum,  $\frac{1}{2}$  gr. of pill of mercury and  $\frac{1}{2}$  gr. of compound extract of colocynth.

**[P1] Pilulæ Colchici et Hydrargyri Compositæ (B.P.C.).** *Syn.* BRODIE'S GOUT PILLS.

*Dose.*—1 or 2 pills.

Contain  $\frac{1}{2}$  gr. of dry extract of colchicum and  $1\frac{1}{2}$  gr. each of pill of mercury, compound extract of colocynth and extract of rhubarb.

**[P1] Vinum Colchici (B.P.C.).**

*Dose.*—10 to 30 minims (0.6 to 2 ml.).

1 of corm in 5 of sherry-type wine.

Is given in mixtures with alkali and magnesium sulphate.

In gout, controls the inflammation. 30 minims as first dose, then 15 minims every 3 hours. It is not objectionable to the taste.

**Pistia Gout Powder.** *Syn.* POLVERE ANTIGOTTOSE (*Farmania Benedettine, Pistia; Roberts, London*). Stated to contain *Gentiana lutea* 30, *Smilax China* (China root) 30, *Jateorhiza palmata* 20, *Aristolochia rotunda* (birthwort root) 10, *Artemisia Abrotanum* (Southernwood) 10.

**[P1] Colchici Semen (B.P.).**

*Dose.*—2 to 5 grains (0.12 to 0.3 g.).

Contains not less than 0.3% of colchicine. *U.S.P. XI* requires not less than 0.45%; *P. Ital. V* and *P. Belg. IV* 0.4%; *F.E. VIII* 0.45%; *P. Helv. V* 0.5%. *I.A.* requires all preparations to be made from the seed.

**[P1] Extractum Colchici Liquidum (B.P.).** *Syn.* Fluid-extractum colchici.

*Dose.*—2 to 5 minims (0.12 to 0.3 ml.).

Contains 0.3% w/v of colchicine.

**[P1] Mist. Colchici (N.I.F.).** Potassium bicarbonate 15 gr., sodium sulphate 10 gr., liquid extract of colchicum 3 m., peppermint water to  $\frac{1}{2}$  oz.



[P1] **Mist. Colchici c. Sod. Sal.** (N.I.F.).

Sodium salicylate 10 gr., solution of burnt sugar 5 m., potassium bicarbonate 15 gr., liquid extract of colchicum 3 m., peppermint water to  $\frac{1}{4}$  oz.

[P1] **Tinctura Colchici** (B.P.).

*Dose*.—5 to 15 minims (0.3 to 1 ml.). *Fr. Cx.* (1 in 10) has max. single dose 25 minims, max. daily dose 90 minims.

Contains 10% v/v of liquid extract, equivalent to 0.03% w/v of colchicine.

[P1] **Tinctura Colchici Seminis** (U.S.P. XI). *Syn.* TINCTURA COLCHICI, U.S.P. X.

*Average dose*.—30 minims (2 ml.).

Colchicum seed, 1 in 10. Is one third stronger than Tinctura Colchici B.P.

[P1] **Vinum Colchici Seminis** (B.P.C.).

*Dose*.—10 to 30 minims (0.6 to 2 ml.).

Colchicum seed, 1 in 10, in detannated sherry-type wine.

[P1] **Colchici Flos.** The fresh perianth of the meadow saffron. It has similar properties to the corn.

[P1-81] **Colchicina** (B.P.C., *Fr. Cx.*, *F.E. VIII*, *P. Dan.*, U.S.P. XI).  $C_{22}H_{25}O_6N = 399.2$ . *P. Helv. V* has  $\frac{1}{2}H_2O$ . *P. G. VI* has  $C_{22}H_{25}O_6N, \frac{1}{2}CHCl_3$  which contains 87% of colchicine.

*Dose*.— $\frac{1}{100}$  to  $\frac{1}{80}$  grain (0.0005 to 0.002 g.) in a pill. *P. Dan.* and *Fr. Cx.* have maximum single dose  $\frac{1}{10}$  grain; max. during 24 hours  $\frac{1}{8}$  grain approximately. U.S.P. XI average dose  $\frac{1}{100}$  grain.

*Intravenously* has been tried in dose of  $\frac{1}{100}$  grain with sodium iodide and sodium salicylate 1 g. each in 20 ml.

Yellowish flakes, crystals or powder, with a hay-like odour when damped and warmed. It is a weak base, most of its salts being decomposed by water.

**Soluble** 1 in 22 of water with neutral solution, readily in alcohol 90% but less in dehydrated alcohol; very soluble in chloroform, slightly soluble in ether (1 in 155).

Has been used in acute gout, rheumatic gout, asthma, cerebral congestion and uræmia.

**GOUT.** While there is no known cure for gout, colchicine is a most valuable drug for affording symptomatic relief. In the crystalline form this preparation is more reliable than the wine or the tincture of colchicum. For acute symptoms colchicine may be prescribed in amounts of  $\frac{1}{100}$  gr., to be taken every one or two hours until 8, 12, or even 16 doses have been ingested. The symptoms of adequacy are associated with the development of nausea, vomiting, or diarrhœa. It may also be used with advantage during the periods between attacks in a dose of  $\frac{1}{80}$  gr. each day for two or three days each week. The use of colchicine in this amount in several cases for more than two years has not produced any toxic symptoms and is a safe practice.—J. H. Talbott and F. S. Coombs, *J. Amer. med. Ass.*, i/1938, 1977.

[P1-81] **Colchicine Salicylate.**  $C_{22}H_{25}NO_4, C_6H_4OH-COOH = 537.2$ .

*Dose*.— $\frac{1}{100}$  to  $\frac{1}{80}$  grain (0.0005 to 0.002 g.).

A yellowish powder soluble in water, alcohol and ether.

## COLLOIDS

By the term "colloid" is meant a certain condition of matter depending chiefly upon the size of the particles. Thus a **Colloidal Solution** or more correctly a colloidal sol, is a system wherein a solid or liquid (disperse phase) is dispersed in a liquid medium

(continuous phase), the size of the dispersed particles lying between 100 and  $1\mu$ . When the disperse phase is a solid, it is called a suspensoid sol, and when a liquid, an emulsoid sol. Thus the conditions are different from those in an ordinary solution where the solute is present either as molecules or ions or a mixture of the two. Unlike solutions, colloidal sols possess the following properties:—

#### **Electrical Properties.**

The disperse particles are charged positively or negatively. On passing an electric current through the sol, the positively charged particles move towards the cathode and the negatively charged towards the anode. This movement of particles in an electric field is known as Kataphoresis. On the addition of electrolytes, a suspensoid sol becomes unstable owing to the neutralisation of the charge, and the dispersed particles aggregate together and precipitate as larger particles. Precipitation or coagulation of a negatively charged sol is brought about mainly by the positive ion of the electrolyte and *vice versa*. Emulsoid sols are not readily precipitated by electrolytes. When an emulsoid sol is mixed with a suspensoid sol, the emulsoid particles appear to be adsorbed on to the surface of the suspensoid particles, with the result that the mixture is much more stable towards electrolytes. This fact is made use of in the preparation of colloidal metal sols which, alone, are typical suspensoid sols. A trace of added emulsoid sol, such as gelatin, agar, egg albumin, isinglass or acacia, confers stability on the preparation.

Colloids such as gelatin are known as protective colloids. Amongst the sols having positively charged particles are the hydroxides of iron, aluminium and chromium, also the basic dyes such as methylene blue, methyl violet, etc. Negatively charged colloidal sols include those of metals, sulphur, iodine, soap and such acid dyes as congo red, eosin, indigo, fuchsin and resinous sols such as mastic, ginger, podophyllin, guaiacum, etc.

#### **Osmotic Pressure.**

The osmotic pressure of most colloidal sols is very small.

#### **Brownian Movement.**

The dispersed particles in a colloidal sol are in rapid motion, the phenomenon being known as the Brownian Movement. It may be observed in certain fine suspensions (not colloidal) using an ordinary microscope, but in colloidal sols it can only be detected by an ultramicroscope. The presence of Brownian Movement serves to distinguish a colloidal sol from a true solution which does not exhibit it. The movement is caused by the bombardment of the disperse particles by the molecules of the continuous phase.

#### **Tyndall Cone.**

When a parallel beam of light is passed through a colloidal sol, the path of the beam is visible. This again serves to distinguish a sol from a true solution, which does not show this phenomenon. A very similar phenomenon, due to fluorescence, is exhibited by some solutions, but whereas the beam of light made visible by the colloidal particles is polarised, this is not so in the case of fluorescence.

#### **Isoelectric Point.**

Many emulsoid sols, particularly those of amphoteric nature such as proteins, have varying charges on their particles according to the pH of the medium. At an intermediate point, the particles are uncharged. This point is known as the isoelectric point of the colloid, and is usually stated in terms of the pH of the medium. Colloids usually exhibit special physical properties at their isoelectric point, one being that of minimum solubility. This fact is often utilised in their separation from other colloids. Thus insulin is precipitated more easily at the isoelectric point, which lies between pH 5 and pH 6, than at other hydrogen ion concentrations.

#### **Dialysis.**

Graham's original conception of *colloids* as substances which will not dialyse through an animal membrane in contradistinction to *crystalloids* which will so dialyse, no longer holds good to-day. The type of membrane used in the dialysis and the dispersion medium or continuous phase are factors which determine the retention or passage of the disperse phase. Thus a copper ferrocyanide

membrane will hold back particles of molecular size. The process of dialysis is, however, an important process in removing electrolytes from mixtures after their employment as precipitants of colloids. The most useful membrane for general use is transparent cellulose tissue (e.g., Cellophane) in the form of "sausage skins." It may be so obtained in long lengths capable of holding large volumes of liquids. The dialysing surface may be considerably increased by arranging a "skin" of smaller diameter inside a large one, placing the whole system in running water, allowing water also to flow through the central "skin" and placing the mixture for dialysis in the space between the two skins after the manner of a double surface condenser.

### ***Nomenclature of Colloids.***

**Lyophile Colloids.** This term refers to colloids such as gelatin, acacia, etc., which can form a sol by the mere addition of solvent or continuous phase in contradistinction to *lyophobic colloids*, such as the metallic sols, which will not do so, but require special dispersion methods. When water is the continuous phase the terms *hydrophile* or *hydrophobe* are used respectively.

**Colloidal Electrolytes.** Certain substances such as soaps undergo electrolysis in water similar to electrolytes, but one of the ions is a complex, consisting of aggregated molecules and ions. These latter aggregates are called *ionic "micelles,"* and form the colloidal particles of the system. Some colloids, like collodion, have a disperse phase which is neutral or uncharged.

**Gels.** Emulsoid sols may be of two types, those which are simple dispersions of liquids such as oils, and others like gelatin sols and agar, in which the particles are very heavily hydrated. In dilute sols these particles are separate, but as the concentration rises they appear to go in together to form a reticulated or sponge-like mass throughout the continuous phase. In this condition the whole system sets to a semi-solid condition which is known as a *gel*.

### ***Manufacture.***

Colloids are used in therapeutics mainly as metallic or metalloid sols. The processes of manufacture vary very considerably, and many are the subject of patents. In the 19th Edition Vol. I, p. 365, details are given relative to the preparation of sols of aluminium hydroxide, arsenic, bismuth, gold, manganese, selenium, etc., to which reference may be made, and particulars regarding the composition of colloidal solutions of certain elements and compounds are given under individual drugs (see Index). The following are the usual methods employed.

1. *Dispersion by precipitation in the presence of a protective colloid.* The precipitation may be the result of reduction, double decomposition, hydrolysis, etc. The preparation of colloidal silver is typical of this method.

This type of method may be used for the preparation of colloidal calomel, iodine, ferric hydroxide, bismuth, sulphur, selenium, manganese and lead.

2. *Electrical Dispersion.* Electrodes made of the metal to be dispersed are immersed below distilled water, and so arranged as to produce a uniform arc when using a current of 8 amperes at about 110 volts. A small quantity of some protective colloid, such as gelatin, is added, the current switched on, and the arc maintained until the necessary concentration of dispersed metal is reached. This type of method is employed for the preparation of gold, silver and lead sols.

3. *Grinding.* Very fine dispersion may be obtained by a process of wet grinding in so-called colloid mills, although the particles are rarely within the colloid range of sizes. The method is used in the preparation of so-called colloidal calamine, sulphur and silver.

4. *Kataphoresis.* In the preparation of certain colloids such as kaolin, the material is first ground to approximate colloidal dimensions in a mill and some electrolyte such as sodium silicate is added. The silicate ions become adsorbed on the kaolin particles and, on providing an electric field, they move to, and are deposited at the anode.

### ***Therapeutic Properties.***

The value of colloids in therapeutics has been the subject of much controversy. Special properties have been claimed for them because of the very small size of the particles in comparison with an ordinary suspension or emulsion. This greatly reduced size, is said to confer a greatly increased specific surface and surface energy, and therefore greater activity. Where it is intended that a medication shall pass through the skin or have a local skin reaction, then the use of

colloidal medicaments as ointments and lotions, etc., may have a justification. Similarly in the use of adsorbents such as kaolin and charcoal in the treatment of alimentary toxæmia, it is logical to presume that a greater adsorption of toxins, etc., would occur if the size of the particles were of colloidal dimensions. It is, however, difficult to understand how a colloidal sol administered by the mouth can avoid being quickly coagulated thus ceasing to possess a special value. Moreover, because of the use of a protective colloid in a suspensoid sol, it is difficult to assess the value of the preparation. Its action may depend upon the protective colloid present, and may change when a different one is used. This is particularly so when such sols are administered parenterally, the reaction which follows being often due to the non-specific protein of the protective colloid. Moreover, many of the so-called suspensoid sols are not permanent, for the dispersed medicament reacts with the protective colloid to form another entirely different substance. This applies especially in the case of the so-called iodine sols.

Colloidal solutions are supplied commercially under the names **Collobell** (*John Bell, Hills & Lucas, London*), **Collosol** (*British Colloids, London*), **Oscol** (*Oppenheimer, Son & Co., London*). Colloidal solutions are also prepared by most manufacturing chemists.

## COLOCYNTHIS

*B.P.*

*Syn.* COLOCYNTHIDIS PULPA, COLOCYNTH PULP, BITTER APPLE, COLOQUINTIDE, COCOMERO AMARO (*P. Ital. V*).

*Dose.*—2 to 5 grains (0.12 to 0.3 g.). *P. Helv. V* max. single dose 5 grains; max. per day 15 grains. The toxic dose of colocynth is 0.6 to 1 g., and the fatal dose 4 g.

The dried pulp of the fruit of *Citrullus Colocynthis* (Cucurbitaceæ) containing not more than 5% of seeds, and not more than 2% of the outer sclerenchymatous part of the pericarp. Has a markedly bitter taste, is free from starch, and contains only about 3% of fixed oil or less, whereas the seeds contain 15% or more. Is imported from Smyrna (the best) and Spain.

*Antidotes.* Empty stomach by emetics or by stomach tube, using dilute tannic acid solution and leaving some in the stomach. Keep patient warm and give demulcent drinks freely. Stimulants, e.g., brandy,  $\frac{1}{2}$  oz., or aromatic spirit of ammonia,  $\frac{1}{2}$  dr., in water. Opium (tincture) by mouth or by rectum. Saline infusion if necessary.

*Uses.* A drastic cathartic. A frequent ingredient of aperient pills. Since it causes griping it is usually given with hyoscyamus. It is excreted by the kidneys and milk, and should therefore not be given to nursing women.

### **Extractum Colocynthidis Compositum** (*B.P.*).

*Dose.*—2 to 8 grains (0.12 to 0.5 g.).

This is in powder form, made by extraction of colocynth and adding finely powdered aloes, scammony resin, curd soap and cardamom.

### **Pilulæ Colocynthidis Compositæ** (*B.P.C.*). *Syn.* PIL. COCHIA.

*Dose.*—1 or 2 pills.

Each pill contains colocynth  $\frac{3}{4}$  gr., aloes and scammony resin, of each  $1\frac{1}{2}$  gr., with curd soap and oil of clove.

**Pilulæ Colocynthis et Hydrargyri (B.P.C.).***Dose.*—1 or 2 pills.

Each pill contains compound extract of colocynth 2 gr. and pill of mercury 3 gr.

**[P1] Pilulæ Colocynthis et Hydrargyri Compositæ (B.P.C.).***Dose.*—1 to 4 pills.

Each pill contains pill of colocynth and hyoscyamus  $\frac{3}{4}$  gr. and pill of mercury  $\frac{1}{4}$  gr.

[P1] **Pil. Aperiens (N.I.F.).** *Syn.* PIL. HYDRARG. C. COLOCYNTH. ET HYOSCY. Colocynth and hyoscyamus pill 4 gr., mercury pill 1 gr.

**[P1] Pilula Colocynthis et Hyoscyami (B.P.).***Dose.*—4 to 8 grains (0.25 to 0.5 g.).

Contains colocynth, aloes, scammony resin, curd soap, dry extract of hyoscyamus, and oil of clove with syrup of liquid glucose.

[P1] **Pulvis pro Pilula Colocynthis et Hyoscyami** consists of the ingredients of the pill less the syrup of liquid glucose. Is more convenient for dispensing.

**[P1] Hamilton's Pill.**

Compound extract of colocynth 2, extract of hyoscyamus 1, made into 4-grain pills. Stated to be less griping than the preceding.

**[P1] Pilulæ Hydrargyri Subchloridi, Colocynthis et Hyoscyami (B.P.C.).** *Syn.* ZITTMANN'S PILLS.*Dose.*—1 or 2 pills.

Each pill contains mercurous chloride 1 gr., compound extract of colocynth  $2\frac{1}{2}$  gr., dry extract of hyoscyamus 1 gr.

**Pilulæ Hydrargyri Subchloridi et Colocynthis (B.P.C.).***Dose.*—1 pill.

Each pill contains compound extract of colocynth 4 gr. and mercurous chloride 1 gr.

**Tinctura Colocynthis (P.G. VI).**

*Dose.*—3 to 15 minims (0.2 to 1 ml.). Maximum single dose 1 g.; maximum daily dose 3 g.

1 in 10 of alcohol (90%). *P. Ital. V* is also 1 in 10 using 80% alcohol.

[P1] **Elaterium (B.P.C.).** *Dose.*— $\frac{1}{10}$  to  $\frac{1}{4}$  grain (0.006 to 0.03 g.), usually in pills.

The dried sediment from the juice of the nearly ripe fruit of *Ecballium Elaterium* (Cucurbitaceæ). A powerful hydragogue cathartic, useful in renal or cardiac disease complicated with dropsy. Its action is variable owing to the fluctuating content of elaterin.

[P1] **Tinctura Elaterii Composita.** *Dose.*—10 to 30 minims.

Elaterium in powder 1, chloroform 50, macerate 2 days, then add alcohol (90%) 200 and compound tincture of cardamom 250, macerate 5 days more and filter. Is more active than a corresponding dose of the powder.

[P1] **Elaterinum (B.P.C.).** *Syn.* MOMORDICIN.  $C_{28}H_{42}O_7$ . *Dose.*— $\frac{1}{10}$  to  $\frac{1}{4}$  grain (0.0015 to 0.006 g.). The crystalline neutral active principle (to extent of at least 20%) of elaterium, insoluble in water, soluble in chloroform (about 1 in 12) and sparingly in alcohol. It is used for the same purposes as elaterium but should be employed with caution, since large doses may cause dangerous prostration.

[P1] **Pulvis Elaterini Compositus (B.P. 1898).** *Dose.*—1 to 4 grains. Elaterin 1, lactose 39.

## COLOPHONIUM

*B.P., U.S.P. XI, Fr. Cx., P. Jap. V, P. Helv. V, P. Dan.*

*Syn. RESIN, ROSIN.*

The residue after distilling the volatile oil (oil of turpentine) from the oleoresin of species of *Pinus*. **Soluble** in alcohol 90%, ether, benzene, carbon disulphide, and light petroleum.

**Ceratum Resinæ** (*U.S.P. XI*).

Resin 3·5, beeswax 1·5, lard 50.

**Heusner's Glue.** Resin (commercial) 50, Venice turpentine 5, methylated spirit 50, benzene 25. For applying extension in fractures.

The following have also been suggested:—

(1) Dammar 250, castor oil or linseed oil 30, benzene 700, sodium bicarbonate 50, amyl acetate a few drops.

(2) Colophony 300, Venice turpentine 20, castor or linseed oil 10, benzene 700, sodium bicarbonate 60, amyl acetate a few drops. *See also Brit. med. J.*, i/1925, 441, and Mencièr's solutions.

**Spiritus Adhesivus Resinosus** (*P. Svec. X*). Terebinthina (*i.e.*, common frankincense from *Pinus* var. *esp. P. pinaster*) 7·5, colophony 18·5, alcohol (90%) 4.

**Unguentum Colophonii** (*B.P.C.*). *Syn. UNGUENTUM RESINÆ, YELLOW BASILICON OINTMENT.*

Colophony 26%, with yellow beeswax, lard and olive oil.

**Copal** (*B.P.C.*). *Syn. GUM ANIMI.*

A fossil resin from *Trachylobium Hornemannianum* (*Leguminosæ*), occurring in pale yellow to reddish masses, entirely **soluble** in alcohol, partially soluble in benzene, glacial acetic acid, ether, chloroform and oil of turpentine. It is used in the manufacture of varnishes.

This is Zanzibar copal. Indian copal is from *Vateria indica* (*Dipterocarpaceæ*), and Brazilian is from *Hymenaea* species and other plants. Australian copal is Gum Kauri, *q.v.*

**Æther Copalis** (*R.D.H.*) (Copal Solution). Copal 1, ether 1, dissolve. For covering cement fillings to protect from the saliva.

**Dammar** as used in this country for varnish making and for microscopic work is the East Indian Dammar from various species of *Shorea*, *Hopea* and *Balanocarpus* (*Dipterocarpaceæ*). It occurs in small yellow nodules, about 3 to 6 mm. in diameter. It is partially soluble in alcohol and soluble in chloroform.

**Elemi** (*Fr. Cx.*). An oleo-resin obtained from *Canarium commune* in soft yellowish, granular masses. *Fr. Cx.* also includes a purified variety.

**Guaiaci Resina** (*B.P.C., P. Helv. V*).

**Dose.**—5 to 15 grains (0·3 to 1 g.).

The resin obtained from the heartwood of *Guaiacum officinale* and of *G. sanctum* (*Zygophyllaceæ*), in rounded tears often covered with a green powder.

**Soluble** almost completely in ether, chloroform, dehydrated alcohol, and in sal volatile and alkalis.

**Uses.** Diaphoretic, diuretic and slightly laxative. It is of value in subacute and chronic rheumatism and in inflammatory conditions of the pharynx and tonsils associated with these affections; also as a gargle in quinsy and follicular tonsillitis. Combined with purgatives it is useful in gout and sluggish liver.

For dysmenorrhœa, 10 gr. of the resin 3 times a day. If this causes flatulence or colic add to each dose 1 gr. of Dover's powder. The patient should begin taking it a week before the period.

**Confectio Guaiaci Composita (B.P.C.).** *Syn.* CHELSEA PEN-SIONER. *Dose.*—1 to 2 drachms (4 to 8 g.).

Guaiacum resin 1%, rhubarb 2%, sulphur 14.5%, with potassium acid tartrate, nutmeg and honey.

**Jephson's Powder.** Precipitated sulphur 2, guaiacum resin 1. For tonsillitis, acne and constipation.

**Mistura Guaiaci (B.P.C.).** *Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.). Contains about 11 gr. of guaiacum resin per oz.

**Tabellæ Guaiaci et Sulphuris (B.P.C.)** contains 3 gr. each of sulphur and guaiacum resin.

**Tinctura Guaiaci (B.P.C.).** *Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.). 1 in 5.

**Tinctura Guaiaci Ammoniata (B.P.C.).**

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

1 in 5, in an ammonia-alcohol solvent with oils of lemon and nutmeg.

This is very useful where the uvula and fauces are enlarged. When dispensed in mixtures the resin must be suspended with 1 in 8 of mucilage of tragacanth.

**Trochisci Guaiaci Resinæ (B.P.C.).** Contain 3 grains of guaiacum resin with fruit basis.

**Kauri Gum.** A resin obtained from *Dammara Australis* in Australia and New Zealand. **Dental Compo** contains kauri gum. This is used for taking impressions when making dentures.

**Lacca (B.P.C.).** SHELLAC. A resinous substance formed by a scale insect, *Tachardia lacca* (fam. Coccidæ, ord. Hemiptera), which lives on a variety of trees, e.g., *Butea frondosa*, *Ficus religiosa*, *Schleichera trijuga*, *Shorea robusta* (Wild Lac). The plants specially cultivated for lac are *Acacia arabica* and *Cajanus indicus*. An ammoniacal solution has been used for the enteric coating of pills, capsules, etc.

**Mastiche (B.P.C., P. Helv. V, P. Dan., P. Belg.).** *Syn.* MASTIC.

*Dose.*— $\frac{1}{2}$  to  $\frac{3}{4}$  drachm (1 to 3 g.).

A resinous exudation obtained by puncturing the bark of *Pistacia Lentiscus* (Anacardiaceæ). In small, hard yellowish tears becoming plastic when chewed.

**Insoluble** in water, partly soluble in alcohol 90%, also soluble 2 in 1 of ether and 2 in 1 of chloroform, readily in acetone.

**Alcohol Mastichi (R.D.H.).** Mastic 2, alcohol 90% 1; dissolve. Harvard Liquid is similar; this is employed for covering a cotton-wool dressing so as to form a temporary dental covering, e.g., during the treatment of canals.

**Benzo Mastiche (Martindale, London).** A solution of mastic in benzene (with other ingredients) for wounds and general surgical use.

The temporary first-aid bandage, if any, is removed and the wound, even if blood-smear, is painted straight away with a sufficient covering of the preparation, and then a dressing applied. Slight injuries may have a layer of sterile gauze first to draw off the wound secretion. Useful in burns and corrosions of the 2nd and 3rd degree, the whole area being painted over and covered with cotton wool.

**Microscopic Varnish.** Mastic  $\frac{1}{2}$  oz., caoutchouc 15 gr., chloroform 2 oz.; macerate and filter.

[P2] **Tinctura Ammoniacæ Composita (B.P.C.).** *Syn.* EAU DE LUCE.

Contains 1½% of mastic with oil of lavender, alcohol 90% and strong solution of ammonia.

**Sandaraca (B.P.C., Fr. Cx., P. Jap. V).** *Syn.* SANDARAC, GUM JUNIPER. A resin obtained by incision from the stem of *Tetraclinis articulata* (Cupressacæ). Brittle, pale yellow tears which do not agglomerate when chewed. Used in pill varnishes.

**Sanguis Draconis** (B.P.C.). *Syn.* DRAGON'S BLOOD. A resinous secretion on the fruits of *Demonorops propinquus* and other species (Palmae). In dull red pieces or lumps weighing up to several pounds. Used for colouring varnishes and in zinc line engraving to protect those parts not to be etched.

**Oleum Succini** (B.P.C.). *Syn.* OIL OF AMBER, OLEUM SUCCINI RECTIFICATUM.

*Dose.*—1 to 3 minims (0.06 to 0.2 ml.).

A yellowish liquid with penetrating odour obtained by the destructive distillation of resins, or by distilling resin oil. Has been given on sugar for asthma and whooping-cough. Used in liniments for its rubefacient properties.

**Linimentum Succini Compositum** (B.P.C.). Oil of amber and oil of clove 25% *v/v* of each in olive oil.

## CONIUM

[P1] "*Alkaloids, the following; their salts, simple or complex:—Coniine.*"

[S1] "*Alkaloids, the following; their salts, simple or complex:—Coniine except substances containing less than 0.1% of coniine.*"

[P1-S1] **Conium Folium** (B.P.C.). *Syn.* HEMLOCK LEAF.

*Dose.*—2 to 8 grains (0.12 to 0.5 g.).

The fresh leafy tops of *Conium maculatum* (Umbelliferae). The leaves contain about 0.2% of total alkaloids chiefly coniine.

**Incompatibility.** Conium preparations are incompatible with alkalis and preparations containing tannin.

**Antidotes.** Empty stomach by emetic or by stomach tube, using dilute tannic acid solution. Leave some tannic acid in the stomach as an antidote, or give medicinal charcoal, stirred up in water. Keep patient lying down and warm. Artificial respiration and oxygen with 7% carbon dioxide inhalations may be necessary. Stimulants, *e.g.*, brandy  $\frac{1}{2}$  oz., or aromatic spirit of ammonia,  $\frac{1}{2}$  dr., in water. Strychnine,  $\frac{1}{2}$  gr., or caffeine sodium benzoate, 2 gr., hypodermically.

**Uses.** Conium and coniine act as direct sedatives to the respiratory centre; in poisonous doses death is caused by asphyxia. Employed in spasmodic affections, especially for whooping-cough and asthma; in neuralgia, epilepsy, and as a sedative in acute mania. Externally it is employed as a soothing application in hæmorrhoids, pruritus ani and anal fissure.

[P1-S1] **Extractum Conii** (B.P.C.). *Dose.*—2 to 6 grains (0.12 to 0.4 g.).

A soft extract prepared from the expressed juice.

[P1-S1] **Succus Conii** (B.P.C.). *Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

The expressed juice preserved with alcohol.

[P1] **Unguentum Conii** (B.P.C.). *Syn.* HEMLOCK OINTMENT.

Extract of coniium 7% in glycerin and simple ointment. Gives relief in pruritus ani and painful fissures.

[P1-S1] **Conii Fructus** (B.P.C.). *Syn.* CIGUË OFFICINALE (Fr. Cx.).

*Dose.*—Fr. Cx. gives maximum single dose 0.25 g.; maximum in 24 hours 0.75 g.



Consists of the dried, unripe fruits of *C. maculatum* and contains up to about 2.5% of total alkaloids, mainly coniine. Used chiefly as a source of the alkaloid, but tinctures and extracts have been prepared from it and used in the same way as preparations of the leaf.

[P1-81] *Tinctura Conii*. *Dose*.— $\frac{1}{4}$  to 1 drachm (2 to 4 ml.).

Conium fruit, No. 40 powder, 1 in 5 of alcohol 60%, prepared by percolation, and standardised to 0.1% of coniine.

[P1-81] *Extractum Conii Liquidum*. *Dose*.—5 to 15 minims (0.3 to 1 ml.).

Conium fruit 100, in No. 40 powder, is exhausted with alcohol 60% containing 1.25% of acetic acid (33%), the last portion of percolate concentrated and mixed with the first 85 previously set aside, so as to produce a liquid extract containing alkaloids equivalent to 1% of alkaloidal hydrochlorides.

[P1-81] *Extractum Conii Fructus*. *Syn.* EXTRAIT DE CIGUË (*Fr. Cx.*).

*Dose*.—Maximum single  $\frac{1}{2}$  grain (0.05 g.).

A firm extract produced by extracting the powdered fruits with 70% alcohol at 35°, evaporating the liquor and treating the residual extract with water, evaporating the aqueous extractive, rejecting the portion not dissolved.

[P1-81] *Coniina*. *Syn.* CONINE, CICUTINE, *d*- $\alpha$ -PROPYLPIPERIDINE.  $C_8H_{10}N(C_2H_5) = 127.1$ .

*Dose*.— $\frac{1}{8}$  to  $\frac{1}{2}$  grain (0.001 to 0.01 g.).

An almost colourless liquid with mouse-like odour and acid taste. B.p. about 166°. *Soluble* 1 in 100 of water, and in organic solvents.

Both this and the hydrobromide are very poisonous, and their internal use has been practically discarded.

[P1-81] *Coniinae Hydrobromidum* (*B.P.C.*, *Fr. Cx.*).

*Syn.* CICUTINÆ BROMHYDRAS (*F.E. VIII*).  $C_8H_{11}N, HBr = 208.1$ .

*Dose*.— $\frac{1}{8}$  to  $\frac{1}{2}$  grain (0.004 to 0.016 g.).

*F.E.* specifies single dose  $\frac{1}{8}$  grain (0.001 g.); during 24 hours,  $\frac{1}{4}$  to  $\frac{1}{2}$  grain (0.005 to 0.02 g.). *Fr. Cx.* has max. single dose  $\frac{1}{2}$  gr., max. in 24 hours  $1\frac{1}{2}$  gr. approx.

Colourless crystalline prisms *soluble* 1 in 2 of water and 1 in 3 of alcohol 90%.

*Scoparium* (*B.P.C.*). *Syn.* BROOM TOPS, GENÊT A BALAIS (*Fr. Cx.*), SCOPARIÏ CACUMINA.

The fresh or dried tops of *Cytisus scoparius* (*Leguminosæ*). Contains the alkaloids sparteine, genisteine and sarothamnine. Is mildly diuretic in cardiac dropsy.

*Decoctum Scoparii* (*B.P.C.*). *Dose*.—2 to 4 ounces (60 to 120 ml.). 1 in 20. *Decoctum Scoparii Concentratum* (*B.P.C.*). *Dose*.—2 to 4 drachms (8 to 16 ml.). 1 in 2½. Is eight times the strength of the fresh decoction.

*Infusum Scoparii Concentratum* (*B.P.C.*). *Dose*.—1 to 2 drachms (4 to 8 ml.). 1 in 1½. Is eight times the strength of the fresh infusion.

*Infusum Scoparii Recens* (*B.P.C.*). *Dose*.—1 to 2 ounces (30 to 60 ml.). 1 in 10.

*Succus Scoparii* (*B.P.C.*). *Dose*.—1 to 2 drachms (4 to 8 ml.). The juice expressed from the fresh plant, preserved with alcohol.

*Scoparin*,  $C_{15}H_{21}O_{11}$ , a phenolic body in broom tops. Has definite diuretic action in doses of 5 to 8 grains.

*Sparteina*.  $C_{15}H_{25}N_2$ . A volatile liquid alkaloid obtained from broom. Is colourless when fresh, darkening on keeping.

Sparingly soluble in water, soluble in alcohol 90%, chloroform and ether.

The pharmacological action of sparteine and related alkaloids.—R. St. A. Heathcote, *J. Pharmacol.*, June, 1926, 431.

**Sparteinae Sulphas** (*B.P.C.*, *Fr. Cx.*, *P. Helv. V*).

$C_{15}H_{25}N_2 \cdot H_2SO_4 \cdot 5H_2O = 422.4$ . *Dose*.—1 to 2 grains (0.06 to 0.12 g.). *Fr. Cx.* has max. single dose  $1\frac{1}{2}$  grain, max. during 24 hours 5 grains.

In colourless crystals. *Soluble* 2 in 1 of water, and about 1 in 5 of alcohol 90%.

**Uses.** Much less poisonous than coniine but similar in action. Resembles digitalis in its action on the heart and is of value in myocardial degeneration. The effect is cumulative owing to slow excretion. With potassium iodide is given in hypertension. It has a marked diuretic action, probably acting through the heart, and is effective in dropsy and post-operative retention of urine. Has been used as a sedative in the withdrawal treatment of opium and morphine addiction.

**Viscum** (*B.P.C.*). *Syn.* MISTLETOE, GUI (*Fr. Cx.*).

*Dose*.—10 to 60 grains (0.6 to 4 g.).

The whole plant, *V. album*, growing as a semi-parasite on various trees, especially the apple, poplar and plum. Has vasodilator action and is used in high blood pressure; has also been used in hysteria and chorea. Administered as a soft extract in pills or as infusion, tincture or liquid extract.

Hyperpiesia has been treated by extract of viscum injections intramuscularly (0.05 g. night and morning) and *per os* in pills (0.15 g. night and morning).

In albuminuria said to be of value. Solid extract used, 0.1 to 0.3 g. *per diem*; acting best when blood pressure and tension are high.

**Detensyl** (*Medico-Biological Laboratories, London*). Mistletoe, liver, pancreas and lung. Tablets for use in hypertension and disorders of the menopause.

**Guipsine** (*Leprince, Paris; Bengué, London*). Pills stated to contain 0.05 g. of active principles of fresh mistletoe. It lowers arterial tension due to a central vasomotor action, and is without any depressing action on the heart itself. For use in arteriosclerosis. *Dose*.—6 to 12 daily.

**Hypotensyl** (*Anglo-French Drug Co., London*). Viscum album extract 0.075 g., hepatic extract 0.10 g., pancreatic extract 0.05 g.

*Dose*.—3 to 6 tablets daily for continuous periods of 15 to 20 days with a week's interval between courses. Hyperpiesia.

## COPAIBA

*B.P.*, *U.S.P. XI*, *P. Helv. V*, *P. Dan.*, etc.

*Syn.* BALSAMUM COPAIVÆ, BALSAM OF COPAIBA, COPAHU (*Fr. Cx.*).

*Dose*.—10 to 30 minims (0.6 to 2 ml.).

The oleoresin obtained from the trunk of *Copaifera Lansdorfii* and other species (*Leguminosæ*), imported from the coast of South America.

**Soluble** almost completely 1 in 1 of alcohol 90%; miscible with dehydrated alcohol, ether, carbon disulphide, fixed and volatile oils. Soluble in an equal volume of light petroleum (b. p. 50° to 60°) but precipitated on adding more solvent. That known as Para copaiba is transparent, yellowish and contains 60 to 90% of oil. It is thinner than the Maracaibo variety, which is brownish and somewhat fluorescent and contains about 45% of oil. Sp. gr. about 0.960 to 0.995.

**Uses.** Diuretic and stimulant to mucous membranes, chiefly used for urethral diseases, and occasionally for chronic bronchitis. May produce a red rash. Given emulsified with mucilage or saponified, but best in capsule owing to its disagreeable taste.

**Oleum Copaibæ (B.P.C.).**

**Dose.**—5 to 20 minims (0.3 to 1.2 ml.).

Distilled from the oleoresin. Sp. gr. 0.896 to 0.910.

**Soluble** in its own volume of dehydrated alcohol and about 1 in 20 of alcohol 90%.

Is used for the same purposes as copaiba.

**Liquor Copaibæ (B.P.C.).** Syn. SOLUBLE COPAIBA.

**Dose.**—1 to 2 drachms (4 to 8 ml.), well diluted.

Copaiba 50% dissolved in a potassium hydroxide solution.

**Liquor Copaibæ, Buchu et Cubebæ (B.P.C.).**

**Dose.**—1 to 2 drachms (4 to 8 ml.), well diluted.

Solution of copaiba 80% v/v with liquid extracts of buchu and cubeb.

**Liquor Copaibæ, Buchu et Cubebæ cum Oleo Santali (B.P.C.).**

**Dose.**—1 to 2 drachms (4 to 8 ml.).

Resembles the preceding solution but contains also 10% v/v of oil of sandal wood and 5% v/v of oil of cassia.

**Liquor Copaibæ et Olei Santali (B.P.C.).**

**Dose.**—1 to 2 drachms (4 to 8 ml.).

Contains 80% v/v of solution of copaiba with oils of sandal wood and cassia.

**Cubeba (B.P.C., Fr. Cx., P. Jap. V).** Syn. TAILED PEPPER.

**Dose.**— $\frac{1}{2}$  to 1 drachm (2 to 4 g.) in cachets.

The dried unripe full-grown fruit of *Piper Cubeba* (Piperaceæ) imported from Java. Contains 10 to 18% of volatile oil. It is sometimes added to Ferrier's snuff, q.v.

A stimulant expectorant used in subacute and chronic bronchitis and the late stages of coryza. It also stimulates the mucous membranes of the genito-urinary tract, and has been used in gonorrhœa, prostatitis, leucorrhœa, etc.

**Extractum Cubebæ Liquidum (B.P.C.).** **Dose.**— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.). 1 in 1.

**Oleoresina Cubebæ (B.P.C.).** **Dose.**—5 to 30 minims (0.3 to 2 ml.).

The ether-soluble extractive.

**Tinctura Cubebæ (B.P.C.).** **Dose.**— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

1 in 5 of alcohol (90%). In chronic bronchitis as an expectorant.

**Trochisci Cubebæ (T. H.)** contain  $\frac{1}{2}$  gr. each with fruit paste. **Dose.**—1 every 3 or 4 hours.

**Oleum Cubebæ (B.P.C., P. Helv. V).** **Dose.**—5 to 20 minims (0.3 to 1.2 ml.).

Colourless, pale green or greenish yellow oil, with camphoraceous odour and characteristic taste. Soluble about 1 in 18 of alcohol 90%. Capsules contain 10 minims. For combinations v. Oleum Santali. Used in bladder and urethral affections, also as an inhalation in bronchitis.

**Vapor Cubebæ cum Limone (T.H.).**

Oil of cubeb 40 m., oil of lemon 10 m., light magnesium carbonate 20 gr., water to 1 oz. A stimulant inhalation.

**Oleum Santali (B.P., U.S.P. XI, P. Helv. V, Fr. Cx., P. Jap. V).**

**Dose.**—5 to 15 minims (0.3 to 1 ml.).

Santal or sandal wood oil is distilled by steam under pressure from the wood of *Santalum album* (Santalacæ), the yield being from 1 to 6%. A yellowish oil, with an aromatic odour and pungent taste.

**Soluble** 1 in less than 1 of alcohol 90%, also in ether and chloroform.

**Uses.** Internally in chronic bronchitis, e.g., a few drops taken on a lump of sugar is found to relieve cough without expectoration. Is much employed in the treatment of gonorrhœa and gleet, and is said to be of value in urinary infections due to staphylococcus. It quickly checks the discharge in dose of 15 minims 3 times a day, and with the use of permanganate, zinc and silver nitrate injections gives good results; also in 10 minim capsules, with benzoic and boric acids as adjuvants, for chronic cystitis.

**Mistura Olei Santali.** **Dose.**—1 ounce (30 ml.).

Oil of sandal wood 4, tragacanth, in powder, 1. Mix and add quickly water to 128. Shake well. Aromatic water with syrup may be used.

**Mistura Santali Composita.** **Syn.** NISBET'S SPECIFIC.

**Dose.**— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.) in water or milk thrice daily.

Oil of sandal wood 12 $\frac{1}{2}$  dr., cassia oil 1 $\frac{1}{2}$  dr., pimento oil 40 m., alcohol (90%) 3 $\frac{1}{2}$  oz.

**Capsules of Nisbet's Specific** are prepared containing the oils of  $\frac{1}{2}$  drachm dose of the above in 20-minim capsules.

**Liquor Santali cum Buchu et Cubeba.**

**Dose.**—1 to 2 drachms (4 to 8 ml.) well diluted.

Yellow sandal wood in powder 4, buchu in powder 1, cubeb in powder 1, alcohol 60% g.s. to moisten. Macerate 2 days, percolate with more alcohol and press to obtain 20.

**Liquor Santali Compositus (B.P.C.).**

**Dose.**—1 to 2 drachms (4 to 8 ml.) diluted.

Oil of sandal wood 5% with tincture of cubeb, tincture of buchu, and oil of cinnamon in alcohol 90%.

**Oleum Santali Australiensis (B.P., Fr. Cx.).**

**Dose.**—5 to 15 minims (0.3 to 1 ml.). Australian sandal wood oil is derived from *Eucarya spicata* and is largely used in Australia and other countries. It contains alcohols equivalent to not less than 90% w/w calculated as  $C_{15}H_{24}O$ . This oil might replace the more expensive oil from *S. album*.

**Arheol (Astier, Paris; Wilcox, Jozeau, London).** The purified active principle of sandalwood oil (containing not less than 98% of santalol). Supplied in capsules containing 0.18 g. and 0.5 g. (10 m.). **Dose.**—1 to 2 g. daily. In urinary infections and wherever sandalwood oil is indicated.

**Eumictine (Bengué, London).** Santalol, salol and hexamine. **Dose.**—8 to 12 capsules daily with meals. Gonorrhœa, cystitis, etc.

**Gonoson (Riedel-de Haen, Berlin; Endocrines-Spicer, Watford).**

Sandalwood oil 80%, kava-kava resin 20%. Capsules contain 0.3 g.

**Dose.**—2 capsules 3 to 5 times a day. Gonorrhœa.

**Santal Midy (Laboratoire de Pharmacologie Générale, Paris; Wilcox, Jozeau, London).** Capsules (0.25 g.) of Mysore citrin sandalwood oil containing 92 to

95% santalol. *Dose*.—2 to 4 capsules 3 times a day before meals. Urinary tract affections.

**Savaresse's Membraneous Capsules** (*Evans, Sons, Lescher & Webb, Liverpool*), are prepared with an animal membrane which generally remains entire until they have passed the stomach. They are available containing either *copaiba* 15 m., or *ol. santal. flav.* 10 m.

**Sabal (B.P.C.).** *Syn.* SAW PALMETTO.

*Dose*.—15 grains (1 g.).

The partly dried fruits of *Serenoa serrulata* (Palmæ). Reputed to have stimulant action on genito-urinary mucous membrane and used in gonorrhœa and cystitis.

**Extractum Sabal Liquidum (B.P.C.).** *Syn.* LIQUID EXTRACT OF SAW PALMETTO. *Dose*.—10 to 25 minims (0·6 to 1·5 ml.). 1 in 1.

**Kava (B.P.C.).** *Syn.* KAVA-KAVA, AWA ROOT.

The rhizome of *Piper methysticum* (Piperacæ) from the Polynesian Islands. Used as diuretic and genito-urinary antiseptic. In gonorrhœa it is not equal to *copaiba* or *santal ol.*

**Extractum Kava Liquidum (B.P.C.).**

*Dose*.— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.). 1 in 1.

## CREOSOTUM

*B.P., U.S.P. XI, Fr. Cx., P. Jap. V, P.G. VI, P. Ital. V, P. Belg. IV, P. Helv. V, P. Dan.*

*Syn.* KREOSOTUM, CREASOTE.

[P1] "*Creosote obtained from wood.*"

[83] "*Creosote obtained from wood—in substances containing less than 50% of creosote obtained from wood.*"

*Dose*.—2 to 10 minims (0·12 to 0·6 ml.), increased to 30 or even 60 minims, in capsules, or in cod-liver, almond, or olive oil, or emulsified in oil with *acacia*. If ordered in aqueous mixtures in excess of solubility it may be suspended with mucilage of *traga-canth* or with tincture of *quillaia*.

Is a mixture of phenols—chiefly *guaiacol* and *creosol*. The variety most used is from *beechwood*. It contains a large percentage of *guaiacol*,  $C_6H_4 \cdot OCH_3 \cdot OH = 124 \cdot 1$ . It mixes clear with *glycerin*. It is more soluble in water than the variety from *pine-wood*, which is anhydrous and mixes perfectly with oil of *turpentine*, consisting chiefly of *creosol*,  $C_6H_5 \cdot CH_3 \cdot OCH_3 \cdot OH : 1, 3, 4 = 138 \cdot 1$ , *homopyrocatechin-methyl-ether*. **Commercial creosote** used for timber preservation consists of *naphthalene oils*—a mixture of the heavy oil from coal tar distilling at  $230^\circ$  to  $270^\circ$ , with the residues from the middle oil ( $170^\circ$  to  $230^\circ$ ), after freeing from phenols.

**Soluble** about 1 in 150 of water; miscible with alcohol 90%, ether, and with fixed and volatile oils.

**Incompatible** with silver oxide (*q.v.*). Also with calcined *magnesia* and slaked lime.

**Antidotes.** Treat as for poisoning by phenol, *see p. 807*.

**Uses.** It is a powerful deodoriser, antiputrescent and antiseptic. Taken by the mouth it promotes expectoration and acts as a gastro-intestinal antiseptic. It is used internally to correct fetor, to check sickness, and to allay the cough and improve the general condition in phthisis; capsules of 5 or 10 m. taken after meals are stated to lessen the gastric irritation in bronchiectasis. Externally, it may be employed to fill the cavities of carious teeth and to allay toothache; it is also used in the form of an ointment in various parasitic skin diseases. Inhalations are of value in bronchiectasis, phthisis, bronchitis and whooping-cough.

**ACNE.** Good results when given in doses of not less than 6 minims 3 times a day, but urine should be watched for toxic effects.—A. Whitfield, *Brit. J. Dermat.*, 1934, 257.

**PNEUMONIA.** After a wash-out enema, inject slowly well up the rectum 40 drops of creosote shaken in 2 oz. of warm milk; retain for 2 hours. Repeat if not retained for more than  $\frac{1}{2}$  hour; in adults add 10 drops of tincture of opium. Repeat enema twice in 24 hours. For children under 1 year give 2 to 10 drops, and older children 5 to 10 drops, with extra drop for each year. Almost specific in pneumococcal conditions; prophylactic in post-operative pulmonary complications and clears up catarrhal states prior to operation.—Ian Macdonald, *Brit. med. J.*, ii/1931, 1111. Value queried.—H. Sutherland, *ibid.*, 1198.

**Mist. Creosot. (N.I.F.).**

Creosote 1 m., spirit of juniper 1 m., syrup 30 m., water to  $\frac{1}{2}$  oz.

**Mist. Creosot. c. Pot. Iod. (N.I.F.).**

Creosote 2 m., potassium iodide 5 gr., tincture of quillaia 2½ m., liquid extract of liquorice 30 m., water to  $\frac{1}{2}$  oz.

**Mist. Creosot. Sed. (N.I.F.).**

Creosote 1 m., tincture of chloroform and morphine 5 m., liquid extract of liquorice 20 m., water to  $\frac{1}{2}$  oz.

**Nebula Creosoti Composita.** Creosote 5 minims, cassia oil 5 minims, almond oil to 1 ounce.

**Pilula Creosoti. Dose.**—2 to 6 grains (0.12 to 0.4 g.).

Creosote 1, curd soap, in powder, 1, digested on a water-bath in a wide-mouthed stoppered bottle. As prophylactic against dysentery.

To make a pill containing creosote 2 m. and phenol 1 gr. use white wax 2½ gr. and powdered liquorice 1 gr. Incorporate the phenol, creosote and wax with the powder gently and quickly.

Perles of creosote, 1 or 3 minims in each, with oil, also capsules, 3 and 5 minims, or more, with oil are made.

**Spiritus Creosoti.**

**Dose.**—1 drachm. Creosote 1, alcohol 90% 40. Lessens cough and expectoration in chronic bronchitis and phthisis.

**Syrupus Creosoti Compositus (B.P.C.).**

**Dose.**—1 to 2 drachms (4 to 8 ml.).

Contains 1 minim of creosote per drachm with spirit of chloroform, glycerin, syrup, and syrup of pine.

**Unguentum Creosoti (B.P.C.)** contains 10% of creosote in a beeswax, lard and paraffin basis.

Used in psoriasis and parasitic skin diseases. **Caution.**—Should not be applied to the abdomen, face, or flexor surfaces of the limbs.

**Vapor. Creosot. (N.I.F.).**

Creosote 1 dr., eucalyptus oil 1 dr., liquid paraffin to 1 oz. For use add 1 dr. to a pint of boiling water and inhale the vapour.

**Vapor. Creosot. Ether. (N.I.F.).**

Creosote 2 dr., liquefied phenol 2 dr., spirit of chloroform 2 dr., weak solution of iodine 1 dr., spirit of ether 1 dr.

**Vapor Creosoti (T.H.).**

Creosote 30 m., French chalk 30 gr., water to 1 oz. *C.L.T.H.* has creosote 40 m., light magnesium carbonate 40 gr., water to 1 oz.

A teaspoonful (*C.L.T.H.* a tablespoonful) in a pint of water at 140°F. Useful in chronic congestion of the larynx and trachea, and in ozoena, fetor of breath and syphilitic throats. For phthisis, it is more sedative in its action if mixed with an equal volume of spirit of chloroform, 5 to 20 m. being employed at one time.

**Vinum Creosoti (Fr. Cx.).**

Dissolve creosote 1, in alcohol 90% 9, and add simple syrup 10, and liqueur wine 80 parts, all by weight.

**Calcii Creosotas (U.S.P. XI).**

*Dose.*—4 to 16 gr. (0.25 to 1 g.). *U.S.P. XI* average dose 8 gr., given every 2 to 4 hours, beginning with small doses and increasing gradually.

A mixture of the calcium compounds of the constituents of creosote, containing when dried 40 to 50% of CaO. A dark brown powder with sharp phenolic taste. Partially *soluble* in water, insoluble portion consisting of calcium hydroxide and carbonate.

Used for administration of large quantities of creosote, but the increased tolerance is probably due to slower absorption and excretion. Does not cause nausea and vomiting.

*Calcreose* (*Maltbie Chemical Co., Newark, N.J.*). Preparations of calcium creosotate available as tablets (4 gr.), compound syrup, and solution.

**Creosoti Carbonas (B.P.C., U.S.P. XI, P. Ned. V, F.E. VIII, P. Belg. IV, P. Helv. V, Fr. Cx.).**

*Dose.*—5 to 20 minims (0.3 to 1.2 ml.) or considerably increased. *U.S.P. XI* average dose 15 grains. May be given in capsules or in milk.

A colourless or amber-coloured nearly odourless syrupy liquid, sp. gr. 1.15 to 1.18. *Soluble* in alcohol, chloroform, ether, benzene and fixed and volatile oils; insoluble in water or glycerin.

It contains the carbonates of guaiacol and creosol and decomposes in the alkaline intestinal juices. Has been used in tuberculosis, bronchitis and pneumonia.

**Proposote Capsules** (*Parke, Davis, London*). Contain 5 m. of creosote phenylpropionate. *Dose.*—1 capsule after each meal. Tuberculosis, bronchitis; also in intestinal disorders of bacterial origin.

**Guaiacol (B.P., U.S.P. XI).**

*Dose.*—5 to 10 minims (0.3 to 0.6 ml.). *U.S.P. XI* average dose 8 minims.

Occurs in two forms, liquid and solid, both of which are recognised by *B.P.* and *U.S.P. XI*. The crystals are official in *Fr. Cx.*, *P. Belg. IV*, *P. Ned. V*, *P. Ital. V* and *F.E. VIII*. The liquid is obtained by distillation of wood-tar creosote and consists mainly of *o*-dihydroxybenzene monomethyl ether,  $C_6H_4(OCH_3)OH = 124.1$ . The crystals of the pure ether are obtained synthetically by heating catechol, potassium hydroxide and potassium methylsulphate. M.p. about 28°. No dose is given in *B.P.* for the solid. Both forms resemble creosote in taste and odour.

*Soluble* 1 in 80 of water; miscible with alcohol 90%, ether, glycerin, and fixed and volatile oils.

*Uses.* Guaiacol is an antiseptic, deodorant and antipyretic.

Internally it is better tolerated than creosote, but has less antiseptic potency. In phthisis, particularly in incipient stages, it may be prescribed in capsules (guaiaicol carbonate), or as cordial, *e.g.*, guaiaicol 13.5, compound tincture of gentian 30, alcohol (90%) 250, and sherry to 1000; two teaspoonfuls two or three times a day in water—or as *Mistura Guaiacolis*, *vide postea*. It is also of value in bronchiectasis in capsules containing 5 to 10 m. three times daily after meals. It is sometimes rubbed into or painted on the skin, covered by oiled silk, over rheumatic joints, in orchitis, mumps, pleurisy and neuralgia; begin with 10 minims and increase to 30 or more; do not cover more than the space of the palm of the hand at a time. As a paint for infected tonsils guaiaicol 3 dr. in olive oil to 1 oz. is of value.

**Injections of guaiaicol 5%, and iodoform 1%,** in sterilised olive oil, in doses of 1 ml., increasing to 3 ml., have been used in tuberculosis; they are not free from danger and the drug is better given *per os*.

**LUNG ABSCESS.** Guaiaicol intravenously causes early subsidence of the symptoms and a regression of the pathologic condition in the lung without producing any unfavourable reactions. In a series of 20 cases so treated it was found that the patients felt considerably better in a very short time owing to the subsidence of the fever and cough, and to the decrease of the daily sputum output and loss of its foul odour. Eradication of all foci of infection about the mouth, nose and throat, and moderate restriction of all activities until the roentgenogram shows complete healing is very essential if the results of the treatment are to be permanent. The solution employed is prepared as follows: from 5 to 10 gr. of guaiaicol is dissolved in 2 ml. of ethyl alcohol and 18 ml. of water containing  $2\frac{1}{2}$  gr. of sodium iodide. Kept in a dark container this solution is stable for some months. An intravenous injection of 20 ml. of this solution is given every third or fourth day. The solution is somewhat irritating to the subcutaneous tissues and should be injected only after the blood has welled into the syringe. No tobacco or alcoholic drinks are allowed, and a high caloric diet is instituted.—C. H. Nammack and A. M. Tiber, *J. Amer. med. Ass.*, ii/1937, 330.

**Durant's Injection.** Guaiaicol 5, iodine 1, potassium iodide 10, sterile olive oil 100. In pulmonary phthisis.

**Mistura Guaiacolis** *Dose.*— $\frac{1}{2}$  ounce (15 ml.) thrice daily.

Guaiaicol 1 dr., alcohol (90%) 1 oz., syrup of lemon 1 dr., spirit of chloroform 2 dr., water to 6 oz. Increase guaiaicol by 2 m. each week until a dose of 12 to 15 m. is given thrice daily, and continue for four months or more.

**Mistura Guaiacolis cum Quinina.**

*Dose.*— $\frac{1}{2}$  drachm gradually increased to 2 drachms, well diluted with water, thrice daily after meals.

Guaiaicol 30 to 40 m., quinine hydrochloride 20 to 25 gr., alcohol (90%) 2 oz., compound tincture of gentian 3 oz., water to 8 oz. The small dose of guaiaicol thus given is increased by giving guaiaicol carbonate in capsules.

**Nebula Guaiacolis et Mentholis Composita (B.P.C.).** Guaiaicol and menthol, 2% w/v in light liquid paraffin.

**Unguentum Guaiacolis.** Guaiaicol 1, lanolin ointment (or other suitable basis) 5; useful in orchitis and mumps.

**Vapor Guaiacol Compositus.**

Guaiaicol and terebene of each 2, menthol and thymol of each 1, spirit of chloroform 3. Inhale 5 to 10 minims from an inhaler night and morning. Employed in phthisis.

[D·P1·81] **Fuller's Inhalant.**

Guaiaicol 4, menthol 2.5, Sydenham's laudanum 125, compound tincture of benzoin to 250. Sometimes terebene 4 is added.

**Bronchodermine (Bengué, London).** Guaiaicol, terpinol, eucalyptol, helenine, pine oil. Applied to the back as a liniment in respiratory affections.

**Quinacol (Allen & Hanburys, London).** Quinine with guaiaicol in capsules. *Dose.*—One capsule (4 m.) increasing to 4 or 5, daily; children one capsule (2 m.) increasing to 3 or 4, daily. Phthisis, whooping-cough, bronchitis, etc.



**Guaiacolis Benzoas.**  $C_6H_4 \cdot OCH_3 \cdot O \cdot CO \cdot C_6H_5 = 228.1$ .

*Dose.*—4 to 12 grains (0.25 to 0.8 g.) in cachet.

In small crystals, almost tasteless, nearly insoluble in water.

**Incompatible** with alkalis.

Useful as an intestinal antiseptic and in incipient phthisis (especially for the diarrhoea).

**Guaiacolis Camphoræ.** *Syn.* GUAIACAMPHOL.

$[C_6H_4 \cdot OCH_3 \cdot O]_2(CO)_2C_8H_{14}$  or  $C_{24}H_{28}O_6 = 412.2$ .

*Dose.*—5 to 10 grains (0.3 to 0.6 g.) in cachets or 5-grain tablets.

Soluble only very slightly in alcohol, insoluble in water; for night sweats and diarrhoea of phthisis.

**Guaiacol Carbonas** (*B.P.C.*, *Fr. Cx.*, *P. Jap. V.*, *etc.*).

$(C_6H_4 \cdot OCH_3 \cdot O)_2CO = 274.1$ .

*Dose.*—5 to 15 grains (0.3 to 1 g.), gradually increased. As much as 6 g. has been given to phthisical patients without causing toxic symptoms.

A white crystalline substance, almost tasteless, and with slight odour.

**Soluble** about 1 in 70 of alcohol 90%, and 1 in 20 of ether, readily in chloroform and slightly in benzene; insoluble in water.

**Uses.** In phthisis, improves appetite and lessens cough, expectoration and night sweats, also in typhoid and for bronchitis.

In rheumatoid arthritis, both the subacute and chronic forms, it sometimes arrests the disease, diminishes size and increases movement of joint and relieves pain. To be given in cachets thrice daily in gradually increasing doses until each dose is 15 to 20 grains—to be continued at least twelve months. At the same time a mixture containing 10 grains of potassium iodide in each dose is given.

**Mistura Arthritica** (*C.X.H.*).

Potassium iodide 5 gr., sodium salicylate 5 gr., guaiacol carbonate 5 gr., mucilage of tragacanth 1 dr., chloroform water to 1 oz.

**Tabellæ Guaiacolis Carbonatis** (*B.P.C.*) contain 5 gr. (0.3 g.).

**Guaiacolis Cinnamas.** *Dose.*—5 to 15 grains (0.3 to 1 g.). White insoluble crystals, given in incipient phthisis.

**"Iodised Tincture of Guaiacol"** (*British Drug Houses, London*). *Dose.*—1 drachm twice daily. Used in pleurisy and synovitis of various types, neurosyphilis of the cerebrospinal system, meningitis, etc.

**Tinct. Guaiacol Chlor-Iodide** (*British Drug Houses, London*). *Syn.* G.C.I. An internal antiseptic for treatment of boils, whitlows, tonsillitis, erysipelas, etc.

**Calcium Guaiacolsulphonate.** *Syn.* GUAIACYL. *Dose.*—10 minims (0.6 ml.) of 5% solution or 1 ml. of 10% solution subcutaneously. Local anæsthetic. Has been employed intravenously, 0.33 g. in 20 ml., in tuberculosis and pulmonary affections. This dose is equivalent to  $\frac{1}{2}$  grain of calcium and 3 grains of guaiacol.

**Potassii Guaiacolsulphonas** (*B.P.C.*, *Fr. Cx.*, *P. Ital. V.*, *P. Helv. V.*, *P. Jap. V.*, *P.G. VI.*, *P. Ned. V.*). *Prop. Name.* THIOCOL (*Roche Products, Welwyn Garden City*), available in powder, tablets and syrup.

$C_6H_3(OCH_3)(OH)SO_3K = 242.2$ . The composition given in the *B.P.C.* as  $C_6H_3(OCH_3)(OH)SO_3K(1:2:3)$  is probably

incorrect; *P.G. VI* and *P. Helv. V* describe it as a mixture of (1 : 2 : 4) and (1 : 2 : 5).

*Dose*.—8 to 15 grains (0.5 to 1 g.) thrice daily. Tablets contain 5 grains.

In colourless crystals with slight guaiacol odour, soluble in water, 1 in 6, slightly in alcohol. Contains 52% of guaiacol.

Has been recommended as a sedative expectorant and intestinal antiseptic in phthisis, bronchitis and pneumonia, also for intestinal catarrh.

The commercial product is a mixture of two isomeric substances and consists of 3 parts of the compound with the  $(\text{OCH}_3)_2(\text{OH})$  and  $(\text{SO}_3\text{K})$  group in the positions 1 : 2 : 5 and 1 part of the 1 : 2 : 4 compound (using the notation adopted in the above formula). The 1 : 2 : 3 compound has never been prepared. —A. H. Clark and E. Kirch, *J. Amer. pharm. Ass.*, 1935, 564.

[P1] **Citro-Thiocol** (*Roche Products, Welwyn Garden City*). Each fluid ounce contains Thiocol 24 gr., codeine phosphate  $\frac{1}{2}$  gr., sodium acid citrate 20 gr., chloroform  $\frac{1}{2}$  m., alcohol 7 m., Ext. Glycyrrh. Glyc. 124 m. *Dose*.—One or two teaspoonfuls every two or three hours. Sedative expectorant for all kinds of cough.

**Morson's Soluble Kreosote.**

*Dose*.—Up to 15 grains (1 g.) thrice daily.

A light brown powder, consisting of the potassium salts of sulphonated fractions from beechwood creosote. It contains approx. 50% of total creosol and guaiacol oils and is soluble in water with slight flavour and agreeable after-taste. For bronchial affections.

**Cresival** (*Bayer Products, London*). An aromatic syrupy solution of calcium cresol sulphate. *Dose*.—1 dessertspoonful 3 to 4 times daily; children, 1 teaspoonful 3 to 4 times daily. Expectorant in bronchitis and other lung conditions.

**Guyucose** (*Bayer Products, London*). Liquid "Somatose" (water-soluble meat albumoses) with 7% of calcium guaiacolsulphonate. *Dose*.—3 to 4 teaspoonfuls daily. In broncho-pulmonary affections, pneumonia, tuberculosis, etc.

[P1-84] **Kres-Lumin** (*Bayer Products, London*). Fluid preparation of calcium cresolsulphonate, containing Lumifal  $\frac{1}{8}$  gr. to the teaspoonful. Expectorant and cough sedative.

**Neo-Plasmoid** (*Farnsworth Laboratories, Chicago; A. Tate, London*). An aqueous colloidal suspension of the potassium salt of *o*-guaiacolsulphonic acid,  $\text{C}_6\text{H}_3(\text{OH})(\text{OCH}_3)(\text{SO}_3\text{H})(1 : 2 : 6)$ , with a trace of a colloidal tannate, for the injection treatment of hernia.

**Novocol-Calcium** (*Richter, London*). Calcium guaiacolphosphate in 4 gr. tablets. *Dose*.—1 or 2 tablets thrice daily. In catarrh of the upper respiratory tract, pharyngitis, bronchitis and tuberculosis.

**Resyl** (*Ciba, Horsham*). Preparations containing glycerol-guaiacol-ether. Issued in tablets ( $1\frac{1}{2}$  gr.), syrup and ampoules for intramuscular injection. *Dose*.—Tablets, 3 to 5 daily in water; syrup, 3 to 5 drachms daily; ampoules, 1 every second day for twenty days. Expectorant and antiseptic in acute and chronic affections of the respiratory organs.

## CRESOL

*B.P., U.S.P. XI., Fr. Cx.*

$\text{CH}_3 \cdot \text{C}_6\text{H}_4 \cdot \text{OH} = 108.1$ .

*Syn.* ACIDUM CRESYLICUM, CRESOLUM CRUDUM (*P. Helv. V, P. Dan., P. Jap. V*), CRESOLO GREZZO (*P. Ital. V*), CRESYL, CRESYLIC ACID.

[P1] "Phenols (any member of the series of phenols of which the first member is phenol, and of which the molecular composition

varies from member to member by one atom of carbon and two atoms of hydrogen) except in substances containing less than 60%, weight in weight, of phenols; compounds of phenol with a metal, except in substances containing less than the equivalent of 60%, weight in weight, of phenols."

[P2] "Phenols as defined in Part I of this List (see [P1] above) in substances containing less than 60%, weight in weight, of phenols; compounds of phenol with a metal in substances containing less than the equivalent of 60%, weight in weight, of phenols."

[S3] "Phenols—in Carvacrol; creosote obtained from coal tar; essential oils in which phenols occur naturally; medicines containing less than 1% of phenols; nasal sprays, mouth-washes, pastilles, lozenges, capsules, pessaries, ointments, or suppositories containing less than 2.5% of phenols; smelling bottles; soaps for washing; solid substances, other than pastilles, lozenges, capsules, pessaries, ointments and suppositories, containing less than 60% of phenols; tar (coal or wood), crude or refined; tertiary butyl cresol; thymol."

[S6] "Phenols—specify proportion as the proportion of phenols (added together) contained in the preparation."

"Compounds of phenol with a metal—specify proportion as the proportion of phenols (added together) that the preparation would be calculated to contain on the assumption that the compounds of phenols with a metal had been wholly converted into the corresponding phenols."

**Dose.**—1 to 3 minims (0.06 to 0.2 ml.). U.S.P. XI average dose 1 minim.

A yellowish brown liquid with tar-like odour. It is a mixture of ortho-, meta-, and paracresols, and forms the principal constituent in crude carbolic acids. **Ortho-cresol** (1 : 2) is a deliquescent solid, melting at about 30° and boiling at 191°. **Meta-** (1 : 3) is a colourless liquid, boiling at about 202°. **Para-** (1 : 4) melts at 36° and boils at about 201°. Sp. gr. 1.04 to 1.05.

**Soluble** 1 in 50 of water almost completely. Miscible with alcohol 90%, chloroform, ether, castor oil and glycerin in all proportions. Also miscible with almond and olive oil in all proportions, but to make a clear solution about 1 in 2½ is necessary.

**Antidotes.** Treat as for poisoning by phenol, see p. 807.

**Uses.** The mixed cresols are less potent in action than phenol (considered one-eighth as poisonous) and are used in many respects on analogous lines to the latter. Their odour is a disadvantage. Cresol is valuable for vaporising into the air in the treatment of whooping cough. It is largely employed in the manufacture of lysol (Liquor Cresolis Saponatus B.P.) and other disinfectants as described later. A small proportion (0.5%), preferably freshly distilled, is much used as an antiseptic to add to vaccines and various solutions for injection.

[P2] **Liquor Cresolis Saponatus (B.P.).** *Syn. and Prop. Names.* **LYSOL** (this synonym may be used only in Gt. Britain and Northern

Ireland, the name being a trade-mark in other parts of the world), ACROSYL (*Monsanto Chemicals, London*), JEYSOL (*Jeyes, London*), MARSHALL'S LYSOL (*Lysol, London*), etc.

Consists of 50% *v/v* of solution of cresol in a saponaceous solvent, any formula yielding a product complying with the *B.P.* characters and tests being officially recognised.

Many formulæ have been published—some employing linseed oil, as in the original lysol. Others proceed without heating, making the potash soap first by shaking, adding a proportion of alcohol and finally the cresol little by little. When vegetable oils are used the addition of 4% of alcohol hastens saponification. Others suggest an equivalent smaller proportion of soda instead of potash. The *B.P.* gives a method of preparation from saponified linseed oil, which is satisfactory if the acid value of the oil is not less than 3. The *P.G. VI* method, which can be completed at room temperature, is also satisfactory, *vide infra*. In order to obtain a lysol miscible with water in all proportions, the cresol used should be free from xylenols, although the product then has a lower Rideal-Walker coefficient. The germicidal value of lysol also varies according to the particular soap used in its preparation. Soaps made from linseed oil or castor oil give the highest values, whilst those made with oleic acid give the lowest.

[P2] **Liquor Cresolis Saponatus** (*U.S.P. XI*).

A more uniform preparation than *B.P.* lysol; it contains 50% *v/v* of cresol and is made with prescribed quantities of linseed oil and potassium and sodium hydroxides.

[P2] **Liquor Cresolis Saponatus** (*P.G. VI, P. Jap. V*), is made as follows:—

Add a solution of caustic potash 27 in water 41, with shaking, to linseed oil 120, and then alcohol 12. Shake frequently at room temperature until saponified. Finally, add cresol 200 and shake. (All parts by weight). It may be necessary to allow to stand a day or so.

These solutions are incompatible with acids.

The Lysol Patent specification, 1017/1890 (expired) gives the following methods of preparation:—

(i) Tar oil 100 g., linseed oil 100 g., caustic potash solution (1 in 2) 75 g., alcohol 65 g. Boil with reflux condenser until saponified.

(ii) Tar oil 40 g., common resin 10 g., caustic potash solution 70 g., alcohol 70 g.

Points of value in cresols for making lysol.—N. Glass and A. J. Jones, *Pharm. J.*, ii/1931, 76.

There are several oils (corn, soya bean, coconut) just as desirable as linseed oil for compound solution of cresol. Coconut oil makes a satisfactory product which shows a phenol coefficient from 50 to 100% higher than the coefficients shown by products made from other oils.—P. L. Burrin, A. G. Worton and F. E. Bibbins, *J. Amer. pharm. Ass.*, 1935, 24, 1079.

The preparation of lysol is greatly facilitated by the addition of 4% S.V.M. to the *B.P.* formula.—J. Jackson, *Pharm. J.*, ii/1938, 369.

Saponated solution of cresol can be rapidly prepared in the following way: Dissolve 24 g. of sodium oleate or sodium stearate in 50 ml. of cresol containing 20 ml. of water. Heat with constant stirring to about 65° until solution is effected. Cool and adjust to 100 ml. with water. Mix well. The resultant preparation is light amber in colour, but should be protected from light to prevent darkening.—L. F. Martin and W. A. Prout, *J. Amer. pharm. Ass., Sci. Edn.*, 1940, 327.

[P1] **Vapor Cresolis Compositus** (*B.P.C.*). Creosote 1, oil of eucalyptus 2, oil of Siberian fir 2, cresol to 100.

**Cresineol** (*British Drug Houses, London*). A combination of cineole and cresol in 3 gr. tablets for use as an internal disinfectant.

**Kerol Capsules** (*Napp, London*). Stated to contain an oxygenated diphenyl compound 60 times less toxic than phenol. Used as a gastric and intestinal antiseptic, the intestinal capsules being enteric coated.

[P1] **Trikresol** (*Schering, London*). A preparation of the three cresols, occurring as a colourless liquid slightly soluble in water. For surgical use  $\frac{1}{2}$  to 1% solution, as an eye wash 1 in 1000 to 1 in 2000.

[P1] **Trikresol-Formalin** in the proportion of 4 of Trikresol to 1 of solution of formaldehyde is a useful application as a dental dressing.

### **Chloro-phenolic Antiseptics.**

**Chlorocresol** (*B.P. Add. III*). *Syn.* PARACHLOROMETACRESOL.

$\text{CH}_3\cdot\text{C}_6\text{H}_3(\text{Cl})\cdot\text{OH} = 142\cdot6$ .

Chlorocresol is 6-chloro-3-hydroxytoluene. It is a white, crystalline solid with a slight characteristic odour, and volatile in steam; m.p.  $64^\circ$  to  $66^\circ$ . R.W. coefficient about 13·3.

**Soluble** 1 in 250 of water, 1 in 50 of boiling water; more soluble in solutions of soap and in caustic alkalis; also soluble in organic solvents, terpenes and fixed oils.

**Parachlorometaxylenol.**  $(\text{CH}_3)_2\text{C}_6\text{H}_2(\text{Cl})\cdot\text{OH} = 156\cdot6$ .

Parachlorometaxylenol is 2-chloro-5-hydroxy-*m*-xylene, a white crystalline solid; m.p.  $115^\circ$ . R.W. coefficient about 36.

Slightly **soluble** in water, a concentrated solution at  $15^\circ$  containing about 3 parts per 10,000. It is more soluble in solutions of soap and in caustic alkalis; also soluble in organic solvents.

**Uses.** Both chlorocresol and *p*-chloro-*m*-xyleneol are being increasingly used as antiseptics and germicides. They possess powerful bactericidal properties and relatively low toxicities, and the disadvantage of low solubility in water is overcome for purposes of use as general antiseptics by dissolving them in solutions of soaps. They are recommended for preserving pharmaceutical preparations, including solutions for hypodermic injections, chlorocresol proving more suitable for this purpose, as its solubility is sufficient to allow the use of the 0·25% solution, which is recommended.

Except in the case of solutions made with alkali, *p*-chloro-*m*-xyleneol shows coefficients nearly twice as great as those shown by *p*-chloro-*m*-cresol. Its great insolubility in water and the consequent necessity for higher concentration of substances to aid dissolution, so reduce the activity of its solutions as to make their efficiencies comparable with those of solutions of *p*-chloro-*m*-cresol. For practical purposes, therefore, the latter compound must be considered the more generally applicable.—N. F. Rapps, *J. Soc. chem. Ind., Lond.*, ii/1933, 175 T.

*p*-Chloro-*m*-cresol in a concentration of 0·05% was found to be approximately equivalent in germicidal power to 0·5% of phenol and 0·3% of Trikresol. *p*-Chloro-*m*-xyleneol and benzyl-*o*-chlorophenol were also tested, but their slight solubility in water precludes their use as preservatives of aqueous solutions of medicaments.—H. Davis, *Quart. J. Pharm.*, 1935, 683.

The preparation of solutions of morphine salts for hypodermic injection containing *p*-chloro-*m*-cresol as preservative.—H. Davis, *Quart. J. Pharm.*, 1935, 683.

It is suggested that for such medicaments as will withstand steaming ( $98^\circ$ ) for 30 minutes, the inclusion of either 0·25% of *p*-chloro-*m*-cresol or 0·001% of phenylmercuric nitrate will provide a big margin of safety against viable bacterial contamination.—H. Berry, E. Jensen and F. K. Siller, *Quart. J. Pharm.*, 1938, 729.

0·25% of *p*-chloro-*m*-cresol is more lethal than 0·5% of phenol or 0·3% of Trikresol, and is much more bactericidal if the substance is acid. Like other

similar substances the action is much diminished by mild alkalinity. Experiments are described in this paper on the use of *p*-chlor-*m*-cresol in low temperature sterilisation, and it is suggested that this use points to new sterilisation procedures of great efficiency involving relatively low temperatures that can be carried out without special apparatus such as autoclaves. A suggested process consists of dissolving or suspending the medicament in distilled water, glucose solution or physiological saline, to which has been added 1 in 400 of *p*-chlor-*m*-cresol, transferring to the final containers and tyndallising or heating to 80° for four hours or to 100° for one hour. Like phenol and cresol, *p*-chlor-*m*-cresol is absorbed by rubber, and this must be borne in mind when products are sent out in rubber-capped bottles.—C. E. Coulthard, *Pharm. J.*, i/1939, 79.

*p*-Chlor-*m*-cresol 0.1% is recommended as a preservative for hypodermic injections. It is more efficient than phenol 0.5%; the ultimate concentration in the injection is only one-fifth of that of phenol 0.5%, and it is less caustic and toxic than phenol.—H. Davis, *Quart. J. Pharm.*, 1940, 47.

**Toxicity.** Experiments on rats and mice showed that phenol and *p*-chlor-*m*-cresol in concentrations of the same order as those suggested for use in sterilisation appeared to be relatively innocuous. It seems unlikely, therefore, that toxic reactions would follow the injection of such concentrations of *p*-chlor-*m*-cresol into patients.—W. A. Broom, reported by C. E. Coulthard, *Pharm. J.*, i/1939, 79.

*p*-Chlor-*m*-cresol has been shown to have about the same order of toxicity as phenol. The 0.25% solution which is recommended for use is unlikely, therefore, to be more toxic than the 0.5% solution of phenol, which is widely used in pharmaceutical injections.—R. Wien, *Quart. J. Pharm.*, 1939, 212.

The introduction of the chlorine atom into the phenol molecule results in compounds having a markedly different mode of toxic action from that of phenol. According to the minimal product of the concentration and survival time, which measures toxicity in its range of most powerful action, the relative toxicity of the chlorophenols as compared with phenol is as follows:—*Ortho* 1.15; *meta* 1.51; *para* 1.89.—W. A. Gersdorff and L. E. Smith, *Amer. J. Pharm.*, 1940, 197. The bromophenols investigated similarly gave the following figures:—*Ortho* 1.25; *meta* 1.56; *para* 1.86.—*ibid.*, 1940, 316.

**Liquor Antisepticus (N.I.F.).** *p*-Chlor-*m*-xylenol 44 gr., ricinoleic acid 75 m., triethanolamine 75 m., ti-tree oil 29 m., industrial methylated spirit 144 m., water to 2 oz.

**N.B.** Distinguish this preparation from Liquor Antisepticus (B.P.C.).

**Parachlorphenol.**  $C_6H_4Cl \cdot OH = 128.5$ . Crystalline needles soluble in alcohol and ether, but not in water to any extent. M.p. 37°, b.p. 217°. Liquid *p*-chlorphenol is practically identical and is used similarly. The *ortho* body boils at 176° and the *meta* melts at 28.5° and boils at 212°.

A powerful antiseptic used in the treatment of lupus, phthisis, keratitis, iritis and in dental work as an analgesic. A filling is made with cobalt and tropacocaine hydrochloride equal parts, with enough *p*-chlorphenol and zinc oxide to produce a paste. The unpleasant taste may be moderated by menthol. 5 to 10% in glycerin has also been used for laryngeal catarrh. Inhalations  $\frac{1}{2}$  to  $\frac{3}{4}$ %.

**C.M.X. Antiseptic (Wyleys, Coventry).** Non-toxic and non-irritant germicide containing *p*-chlor-*m*-xylenol in a saponaceous solution of essential oils.

**C.M.X. Obstetric Cream.** A water-soluble ointment for use as an antiseptic in midwifery. **C.M.X. Pessaries.** Antiseptic pessaries containing C.M.X.

**Dettol (Reckitt & Sons, Hull).** A non-toxic, non-irritant antiseptic stated to consist of a halogen derivative of xylene dissolved in a mixture of aromatic essential oils with a neutral solution of a suitable soap. For use in surgery, gynaecology, obstetrics, and for instrument sterilisation, etc. R.W. Coefficient, 3.

**Dettol Obstetric Cream.** A non-greasy ointment for use as an antiseptic in midwifery. **Dettolin.** A concentrated mouthwash stated to contain dimethyl-chlorophenylhydrate 1.02%, menthol 0.12%, *sapo vegetalis* 0.5%, tinct. roseum aromatica 64.9%, elixir glusidi (B.P.C.) 6.0%, water to 100.

A 1% solution of Dettol kills hæmolytic streptococci and *B. coli* even in the presence of pus, and its bactericidal activity is little diminished by admixture with soap. It may be used in concentrated form without toxic effects and is well tolerated by the hands, vulva and even the intact vaginal mucous membrane.—*Brit. med. J.*, ii/1933, 275.

**N.P.A. (Richter, London).** A non-poisonous antiseptic containing *p*-chlor- $\alpha$ -naphthol emulsified with antiseptic essential oils. R.W. coefficient 3.4 to 3.5.

**Zant (Evans, Sons, Lescher & Webb, Liverpool).** A non-poisonous antiseptic containing *p*-chlor-*m*-xylenol emulsified with pine and other essential oils. Also available as a catheter lubricant and skin cream.

**Acrosone (Woolley, Manchester), Amphyl (Lysol Ltd., London), Lysantol (Allen & Hanburys, London), Neo-Monsol (Monsol Ltd., London), and Verpine (C. G. Fox, London),** are non-poisonous, non-irritant antiseptics for use in midwifery, for wounds, and as general disinfectants.

### Higher Phenolic Antiseptics.

In general, the bactericidal power of phenol and its homologues increases as the complexity of the alkyl group increases. Thus cresols have a phenol coefficient of about two, whilst that of thymol is about twenty-five. Research on the variation of the phenol coefficient with increase in the alkyl group showed the *n*-amyl derivatives to be always the most active, and the alkylcresols to be more active than the alkylphenols. It was also found that toxicity tends to decrease with rise in molecular weight, amyl-*m*-cresol, for example, with a phenol coefficient of between 200 and 300, having about half the toxicity of hexyl-resorcinol.

**Abracide (A. Boake, Roberts, London)** is tertiary butyl cresol, offered in the form of a lotion, ointment or prophylactic powder for the treatment of fungous diseases of the skin such as athlete's foot, etc.

**Abracyl (A. Boake, Roberts, London)** consists of amyl salicylate rendered germicidal with tertiary butyl cresol for the treatment of minor burns, scalds, etc.

**Cresantol-3 (Monsanto Chemicals Ltd., London)** is a non-poisonous antiseptic stated to consist of substituted phenols containing aryl groups. R.W. coefficient 105.

The following formulæ yield non-poisonous antiseptics, having R.W. coefficient of 3.4:—

**Formula A.** Cresantol-3 3 ml., ti-tree oil 3 ml., oil of lemon grass 0.05 ml., isopropyl alcohol 10 ml., triethanolamine 5 ml., ricinoleic acid 5 ml., water to 100 ml. Mix the triethanolamine with the ricinoleic acid and a little water, stirring vigorously, dissolve the Cresantol-3 and the oils in the alcohol, mix the two solutions and dilute to volume. The product has a pH of 8.8.

**Formula B.** Cresantol-3 3 ml., terebene 2 ml., oil of sassafras 1 ml., industrial methylated spirit 10 ml., potassium hydroxide 10% *w/v* 10 ml., ricinoleic acid 6 ml., water to 100 ml. Heat the potassium hydroxide solution with the ricinoleic acid, dissolve the Cresantol-3 and the oil of sassafras and terebene in the alcohol, mix the two solutions and dilute to volume. The product has a pH of 11.0.—*Pharm. J.*, ii/1936, 273.

**Dimol "43" (Dimol Laboratories, London; Anglo-French Drug Co., London).** Dimethyl-methoxyphenol,  $C_6H_3(CH_3)_2(OCH_3)OH = 152.1$ , in combination with tri- and tetra-methylphenols. R.W. coefficient 43. For use in dysentery, colitis and intestinal toxæmias generally. It is supplied in tablets: A (enteric-coated for solution in the bowel) and B (sugar-coated for solution in the stomach). Also supplied as a syrup, lavage powder, ointment and snuff.

[P1] **Amylmetacresol.**  $C_6H_4 \cdot C_6H_4(OH)CH_3 = 165.13$ .

A colourless solid with a pleasant odour and taste. M.p. 24°. It is almost insoluble in water, but soluble in alcohol, ether and oils.

Amyl-*m*-cresol possesses powerful antiseptic properties (R.W. coefficient 250) and a low toxicity.

[P2] **Amyl-meta-cresol Capsules (Boots, Nottingham).** Each capsule contains 0.15 g. of amyl-*m*-cresol in olive oil. Dose.—2 to 3 thrice daily after meals. In chronic intestinal infection and colitis.

**A.M.C. Antiseptic Solution (Boots, Nottingham).** A concentrated oral disinfectant for use as a mouthwash or gargle containing 1% of amyl-*m*-cresol.

**Kramsol** (*Boots, Nottingham*). An instrument-sterilising solution containing amyl-m-cresol and formaldehyde. Highly germicidal and free from corrosive action.

### Proprietary Phenolic Disinfectants.

(For trade-names of some proprietary lysols, see under *Liquor Cresolis Saponatus B.P.*, p. 465.)

The nomenclature used by manufacturers in describing their preparations includes the following:—

**"Tar Acids."** These are oxygenated hydrocarbons, including phenols, cresols and higher hydroxy compounds.

**"Phenoloids."** A vague term. The bodies so called simply consist of phenol and its higher homologues, i.e., xlenols and dimethylhydroxybenzenes. They are more bactericidal and less poisonous, and they make good emulsions with soap and water.

**"Tar Oils."** The neutral bodies present, i.e., insoluble in soda.

**"Coke Oven Oils."** Contain varying percentages of "phenoloids" with tar oils.

The disinfecting power of the higher phenols increases in proportion to their position in the homologous series, but their solubility decreases proportionately. Bodies, therefore, with the hypothetical diphenyl nucleus which have become so popular can only be used as emulsions.

For various methods used for the determination of cresol and higher phenols in lysols and disinfectants, for meta-cresol in cresol, and for the Chick Martin and Rideal-Walker methods of standardising disinfectants, see Vol. II.

[P2] **Creolin** (*Pearson's Antiseptic Co., London*). Contains 35% of the less toxic but more powerful homologues of phenol. R.W. coefficient 18-20. Used diluted 1-200 to 1-400.

[P2] **Creophen** (*Ferris, Bristol*). A coal tar product containing 25% v/v of phenols, with R.W. coefficient 5-6. Used as a general antiseptic in  $\frac{1}{4}$ -1% solution.

[P2] **Cyllin Medical** (*Jeyes Sanitary Compounds, London*). A saponaceous solution of high boiling phenols with coal tar hydrocarbons in vegetable oil soap. It contains 50-55% v/v of phenols and has R.W. coefficient 22-24. For medical and surgical purposes it is used diluted 1-300. For use in contact with mucous membrane, e.g., douches, 1 in 600.

[P2] **Cyllin Capsules**, containing 1 and 3 minims, keratin-coated, have been given as an internal antiseptic in summer diarrhoea, dysentery, colitis and sprue. "Stomachic" capsules, gelatin-coated, are also available.

**Lano-Cyllin Ointment** contains 5% of Cyllin in a wool fat and soft paraffin base. For eczema, ringworm, hæmorrhoids, etc.

[P2] **Izal Germicide** (*Newton, Chambers, Sheffield*).

A 40% emulsion of Izal oil, containing aromatic hydroxy compounds, including xylenes and related substances obtained from bituminous coal. Izal germicide is miscible with water, saline, alcohol and glycerin. R.W. coefficient 18 to 20. For general purposes dilute 1 in 600; for a mouthwash 1 drop to a tumbler of warm hypertonic saline. A 1 in 200 solution has been officially recommended for the cleansing of service and civilian respirators. [P2] **Izal Oil Capsules** contain 2 m.; for internal antiseptics and in bronchiectasis, etc.

[P2] **Jeyes Fluid** (*Jeyes Sanitary Compounds, London*). A non-irritant and non-corrosive saponaceous solution of cresols and coal tar hydrocarbons with resin and vegetable oil soap. It contains 25-30% v/v of phenols and has R.W. coefficient 6-7.



[P2] **Monzol** (*Monzol Ltd., London*). A non-caustic germicide stated to be prepared from oils obtained in the gasification of coal by the Mond power gas process. It contains 12% of the homologues of phenol, the formula being sulphonated cod-liver oil 17%, curd soap 3%, "Ol Picis (Mond)" 73%, terpinoline 2% and water 5%.

[P2] **Pacolin** (*Pearson's Antiseptic Co., London*). Disinfectant containing 22% of the homologues of phenol. Is employed diluted 1-80 for general purposes, or 3-5 drops in a tumbler of water as a mouth-wash.

## CUPRUM

Cu = 63.57.

**Incompatibles with Copper Salts.** Alkalis and alkaline carbonates, also preparations containing tannin and iodides.

**Antidotes to Copper Salts.** Empty stomach by emetic (if vomiting has not occurred) or by stomach tube. Potassium ferrocyanide, 10 gr. in water, is said to be a useful antidote. Keep patient lying down and warm; apply heat to abdomen. Give white of egg and demulcent drinks freely, but avoid oils and fats. Morphine,  $\frac{1}{2}$  gr. hypodermically, or tincture of opium by mouth, for pain.

**Cupri Sulphas** (*B.P., U.S.P. XI, Fr. Cx., P. Helv. V*).

$\text{CuSO}_4 \cdot 5\text{H}_2\text{O} = 249.7$ .

**Dose.**— $\frac{1}{4}$  to 2 grains (0.016 to 0.12 g.); as emetic, 5 to 10 grains (0.3 to 0.6 g.). Average dose  $\frac{1}{2}$  to  $\frac{3}{4}$  grain (0.016 to 0.03 g.). *Fr. Cx.* has maximum single and daily dose 0.75 g.

Blue crystals. **Soluble** 1 in about 3 of water, 1 in 3 of glycerin; insoluble in alcohol 90%.

**Uses.** Given internally, copper sulphate in small doses has an astringent action and has been employed for this purpose in diarrhoea, cholera and amoebic dysentery (by colonic irrigation). In larger doses it has an emetic action, but it is not generally recommended for this purpose except in the case of phosphorus poisoning, in which it forms an insoluble phosphide and so prevents absorption.

Externally it is astringent and caustic, and has fungicidal properties. Solutions of  $\frac{1}{4}$  to  $\frac{1}{2}$ % have been employed locally as stimulant astringents in eye affections such as conjunctivitis and trachoma, and frequent application of a 1% solution is of value in styas after epilation of the lashes. Copper pencils, prepared by fusing 1 part of potash alum with 2 parts of copper sulphate, are useful for this purpose. 0.5 to 1% solutions have also been employed in urethritis and vaginitis, in tropical ulcer, and as an application to discharging gums in pyorrhoea alveolaris.

It has been employed both by injection and internal irrigation in actinomycosis, using a 1% solution.

**ACTINOMYCOSIS.** Treated by injection of 1% copper sulphate solution every few days until softening of the infiltration occurs. For small lesions a few ml. If extensive, the first injections are given under anæsthetic. Abscesses are opened and scraped and 40 to 100 ml. of  $\frac{1}{2}$  to  $\frac{1}{4}$ % injected.

**AMŒBIC DYSENTERY.** Colonic irrigation recommended with 2 to 4 litres of hot solution of copper sulphate 1 : 5000 at a temperature of 50° to 55° in the container at the rate of 100 to 200 ml. per minute. On arrival in the colon the temperature is 45° to 48°. Ten irrigations daily, or every other day, usually cured the condition.—P. Beregoſſi, *Canad. med. Ass. J.*, i/1935, 641.

**FISTULAS**, both tuberculous and osteomyelitic, have been well treated with injections of 2 to 3 ml. of 10% solution.

**TRACHOMA** has been well treated with subconjunctival injections of a 1% solution of copper sulphate with 4% procaine.

**TROPICAL ULCER.** In local treatment copper sulphate acts with such rapidity in comparison with other forms of treatment that it can be regarded as a specific. It is best used as a 1 in 150 solution, applied as a continuous bath. The first essential in the general treatment is a diet rich in vitamins.—C. E. M. Ganther, *Med. J. Aust.*, i/1938, 348.

**Collyrium Cupri Sulphatis (B.P.C.).** 0.25% w/v.

**Guttæ Cupri Sulphatis (R.L.O.H.).** 1 or 2 grains to the ounce. Suitable as a lotion for gleet.

#### **Alibour Waters.**

**Solutum Cuprozincicum Forte (Fr. Cx.).** *Syn.* EAU DE DALIBOUR FORTE. Copper sulphate 10 g., zinc sulphate 35 g., tincture of saffron 1 g., concentrated tincture of camphor (10% w/w) 10 g., distilled water to 1 litre.

It must be diluted for use with 5 or 6 times its volume of water, as a wet dressing in eczema.

**Solutum Cuprozincicum (Fr. Cx.).** *Syn.* EAU DE DALIBOUR. Copper sulphate 1 g., zinc sulphate 3.5 g., tincture of saffron 1 g., concentrated tincture of camphor 10 g., distilled water to 1 litre.

**Lotio d'Alibour (L.S.H.).** Copper sulphate 2, zinc sulphate 7, camphor water to 100.

**Lot. Cupro-Zincica (N.I.F.).** *Syn.* ALIBOUR WATER.

Zinc sulphate 12 gr., copper sulphate 8 gr., camphor water to 2 oz.

**Lotio Zinci et Cupri Sulphatum (L.H.).**

Zinc sulphate 6 gr., copper sulphate 4 gr., camphor water to 1 oz.

**Pasta d'Alibour (Strong) (L.S.H.).**

Zinc phenolsulphonate 1, copper sulphate 1, precipitated sulphur 5, diatomite 15, zinc oxide 30, lanolin to 100. The weak paste contains 0.1% of zinc phenolsulphonate, 0.5% of copper sulphate and 1% of precipitated sulphur.

**Cuprum Aluminatum (P.G. VI, P. Helv. V).** *Syn.* LAPIS DIVINUS, COPPER ALUM.

Potash alum powdered 16 is mixed with powdered copper sulphate 16 and potassium nitrate 16, and melted with moderate heat in a porcelain dish. Camphor 1 and potash alum 1 are then added and the mass moulded or poured on to a plate to set. It is employed as a mild caustic in ophthalmology.

A preparation known as "Brass Paste," formed by combining basic copper sulphate 86, with basic zinc sulphate 14, has been employed in cutaneous tuberculosis, especially in tuberculous conjunctivitis.

**Cupri Acetas.**  $(\text{CH}_3\text{COO})_2\text{Cu} \cdot \text{H}_2\text{O} = 199.6$ .

Dark green crystals. Applied to ulcers acts as a stimulating caustic. Soluble 1 in 15 approximately of water; only slightly in alcohol. The fatal dose *per os* is said to be 154 to 184 gr., and 154 to 308 gr. of the sulphate.

**Cupri Subacetas.** *Syn.* VERDIGRIS, AERUGO, COPPER OXYACETATE.

Is usually of indefinite composition, approaching  $\text{Cu}(\text{C}_2\text{H}_3\text{O}_2)_2 \cdot \text{Cu}(\text{OH})_2 \cdot 5\text{H}_2\text{O} = 369.3$ . Occurs in blue needles or scales, efflorescing in air and becoming green. Partly soluble in water with decomposition, insoluble in alcohol 90%; soluble in ammonium carbonate solution.

**Linimentum Æruginis (Ph. Lond.).**

A decoction of verdigris, vinegar and honey, employed in veterinary work.

**Cupri Chloridum.** *Syn.* CUPRIC CHLORIDE.  $\text{CuCl}_2 \cdot 2\text{H}_2\text{O} = 170.5$ .

*Dose.*— $\frac{1}{2}$  to 2 grains (0.016 to 0.12 g.).

Greenish very deliquescent crystals. Use similar to that of copper sulphate.

**Cupri Citras** (*P. Jap. V*).  $\text{C}_6\text{H}_5\text{O}_2\text{Cu}_2 \cdot 2\frac{1}{2}\text{H}_2\text{O} = 360.2$ .

Greenish powder slightly soluble in water. Used as an ointment for ulceration and granulation of the eye-lids.

**Unguentum Cupri Citratis** (*R.L.O.H.*).

Copper citrate 20 gr., yellow soft paraffin to 1 oz.

**Cuprentum** (*Allen & Hanburys, London*). 5% of soluble copper citrate in a lanolin base. For ophthalmic use.

**Cupri Nitras** (*B.P.C.*). *Syn.* CUPRIC NITRATE.  $\text{Cu}(\text{NO}_3)_2 \cdot 3\text{H}_2\text{O} = 241.6$ .

Deliquescent blue powder or crystals, very soluble in water and alcohol. Used similarly to the sulphate in astringent lotions.

**Cuprase** (*Ducatte, Paris; Anglo-French Drug Co., London*). Colloidal solution of copper hydroxide in 5 ml. ampoules for very slow intramuscular injection for the treatment of cancer.

## DEXTROSUM

*B.P.*

$\text{C}_6\text{H}_{12}\text{O}_6 = 180.1$ .

*Syn. and Prop. Name.* MEDICINAL GLUCOSE (ANHYDROUS), GRAPE SUGAR, GLYCOSUM (*P. Helv. V*), SACCHARUM AMYLACEUM (*P.G. VI*), GLUCOSE OFFICINAL (*Fr. Cx.*), DEXTROSOL (*Corn Products, London*).

*Dose.*—Up to 6 ounces daily *per os*; intravenously, 250 to 300 ml. of a 10 to 20% solution; rectally, it is given in the form of a 5 to 10% solution. A 33 $\frac{1}{3}$ % solution has been employed intravenously in the treatment of shock following the insulin therapy of schizophrenia (sufficient being given to raise the blood sugar above hypoglycæmic levels), and a 50% solution as a sclerosing agent for varicose veins.

A white crystalline or granular powder obtained by the hydrolysis of starch. It is an equilibrium mixture of  $\alpha$  and  $\beta$  dextrose. The *B.P.* requires not more than 2 $\frac{1}{2}$ % of moisture.

Dextrose monohydrate is also available, and is the form generally used for oral administration, being supplied under the name "medicinal glucose." It is the variety usually required when "glucose" *per se* is asked for. Dextrosium (*U.S.P. XI*) is the monohydrate, but the use of other hydrates is permitted, provided due allowance is made for the extra moisture.

Solid glucose, less pure, is in yellowish masses containing 10 to 20% of bodies allied to dextrin, *viz.*, amylin and gallsin.

**Soluble** 1 in less than 1 of water, 1 in 50 of cold alcohol 95%, 1 in 5 of boiling alcohol 90%; also soluble in glycerin.

**Uses.** Is given orally, intravenously or *per rectum* as a readily absorbed carbohydrate food in wasting diseases. It assists the metabolism of fats and prevents acidosis by raising the glycogen content of the liver. This action is utilised before the administration of drugs which may have a toxic action on the liver, such as cinchophen, neoarsphenamine, chloroform, etc. Before operations dextrose, in the form of barley sugar, may be taken *ad lib.* for

the prevention of post-anæsthetic acidosis, and of delayed chloroform poisoning. Dextrose is widely used in the severe nutritional disturbances of infants, especially when accompanied with diarrhoea and vomiting. Massive doses *per os* are of value in the prevention and treatment of travel-sickness (sea, air or car), and of the vomiting of pregnancy. Hypertonic solutions (25%) are injected intravenously to relieve intracranial pressure by osmosis in meningitis and hydrocephalus, also to assist drainage of the accessory nasal sinuses. Isotonic dextrose is given intravenously as a circulatory stimulant in the treatment of shock and various cardiac diseases.

Concentrated (50% or more) solutions have been used for the injection treatment of varicose veins. It is generally held that recanalisation and pulmonary embolism are more likely to occur with this than with other sclerosants.

**USE IN SURGICAL SHOCK.** In the treatment of surgical shock intravenous injection of dextrose has beneficial effect on the pulse and general strength, and in relief of thirst. By this means, water, the first need, is given in large amount with safety, and sugar to the extent of 2 ounces per diem without any demand upon the alimentary tract. Increased action of the kidneys is caused, and diluted toxic matters are removed.

The solution is also used intravenously with the addition at the time of use of 4 to 8 drops of adrenaline solution.

When a dehydrating effect is required hypertonic solutions are given intravenously or per rectum, since if given subcutaneously such solutions may cause œdema.

Prior to operations on children a full diet is advised and a bottle of barley sugar the day before the operation and more on the morning of the operation; in young infants, when the operation is severe and resistance low, 5% dextrose subcutaneously may be given, and in older children 10% per rectum.

Always *before* a severe operation, (1) when liver efficiency is suspect, (2) when the metabolic rate is high, (3) when patient is under-nourished or emaciated: always *after* a severe operation when blood transfusion is impossible: *after* any anæsthetic (1) when loss of blood has been heavy and blood transfusion is impracticable, (2) in case of shock, (3) when it has not been given before the anæsthetic, (4) when a rough surgeon has operated, or more than the usual amount of anæsthetic has been used, (5) when there is a history of epilepsy.—F. P. de Caux, *Brit. med. J.*, ii/1929, 1005. (10% solution is preferred by this writer, given at 100°F.)

Intramuscularly a 10% solution in saline is relatively safe for raising blood sugar and when other methods contraindicated. 20 to 40 ml. for infants; 100 ml. for older children or adults. The maximum rise in blood sugar occurs in  $\frac{1}{2}$  hour.—J. Glaser, *J. Amer. med. Ass.*, ii/1928, 726.

The adult body can utilise only 0.8 g. per kilo weight per hour. If given too rapidly it is promptly excreted through the kidneys and wasted.—*J. Amer. med. Ass.*, ii/1929, 1327.

Intravenously for adults, 75 g. in 300 ml. of water has been advised; given during 1½ hours.—*Lancet*, ii/1929, 723. Less, it is stated, will not give the maximum therapeutic effect, and more may produce over-stimulation of the insulin-producing activity of the pancreas. Single repeated doses preferable to prolonged injection. Half dose for a child and quarter dose for infant, but same length of time for injection.—F. Titus and H. D. Lightbody, per *J. Amer. med. Ass.*, ii/1929, 947.

Although the rectal administration of dextrose is a popular measure, there is grave doubt whether absorption of the substance from the rectum does in fact take place. Animal experiments showed that following the injection of dextrose into the rectum the blood returning from this portion of the bowel failed to yield any evidence suggestive of even a slow rate of absorption. On the other hand dextrose injected into the small intestine was rapidly absorbed. Experiments on man showed that glucose administered even at the rate of 30 g. per hour by a continuous drip apparatus failed to cause any rise in the systemic blood dextrose. Even when large amounts were allowed to remain in the bowel for a considerable time, no rise in blood glucose was observed. It is concluded that absorption of dextrose from the human rectum is of no therapeutic value.—A. B. Corkill, per *Practitioner*, ii/1936, 659.

**ANGINA PECTORIS.** Administration of dextrose recommended to improve the coronary circulation and thus increase oxygen supply to the heart. Treatment consists in giving 50 to 100 g. of dextrose orally and 5 to 10 units of insulin subcutaneously daily for 6 to 10 days. The dose is doubled if no improvement is obtained, and is continued until improvement is definitely noted. Alternatively a 10 to 15% solution of dextrose may be given intramuscularly or a 25% solution intravenously.—R. L. Chopra, per *Prescriber*, 1939, 327.

**ARTHRITIS, CHRONIC.** From 20 to 60, or even 100 ml. of 10% dextrose into the painful areas of the muscle and subcutaneous tissues gives immediate relief of pain in muscular rheumatism and lumbago. Also used with success in sciatica, etc.—*Brit. med. J. Epit.*, ii/1931, 8.

**DIABETES.** Diabetic uræmia cured by intravenous injection of a pint of 25% dextrose solution in normal saline, repeated in 24 hours.—H. W. Fullerton and co-workers, *Lancet*, i/1932, 559.

**JAUNDICE.** Intravenous injection of 500 ml. of a 10% dextrose solution may be indicated two or three times a day to rehabilitated patients with abnormally functioning livers. In jaundice, intravenous injections of 5 ml. of a 10% solution of calcium chloride help to hasten coagulation of blood, prevent post-operative bleeding and neutralise the toxic bile pigments.

**PNEUMONIA.** Intravenous injections of 10% dextrose are most valuable when circulatory failing has commenced.

**SEPTICÆMIA.** Continuous giving of dextrose, up to 3 litres a day, drop by drop into the tissue of the breast, or into the saphenous vein, of great value in severe cases.—Sir W. Wheeler, *Lancet*, ii/1931, 245.

**TOXÆMIA** with gastric stasis well treated by intravenous injections of 10 g. (1%) sodium chloride, and 100 g. dextrose (10%), in 1000 ml. freshly distilled sterile water. Twenty minutes allowed for injection, 1, 2 or 3 litres being injected daily, supplemented by hypodermoclysis and proctoclysis.

**VARICOSE VEINS.** A mixture of 50% dextrose and 30% sodium chloride thought to be the ideal solution. *Dose.*—2 to 10 ml.—not more than 20 ml. at one sitting, with injections every other day.—H. M. Kern and L. W. Angle, *J. Amer. med. Ass.*, ii/1929, 601.

A 50% solution found the blandest and most efficient method of sclerosing. Inject 5 to 10 ml. and then again 3 to 4 cm. higher; repeat bi-weekly.—G. de Takats, *J. Amer. med. Ass.*, i/1929, 778.

Up to 5 ml. of 66% solution. There is a tendency for the clot to break up, and of the recorded instances of pulmonary embolism from varicose vein injections, the majority have occurred with dextrose.—W. Levi, *Lancet*, ii/1930, 16.

20,000 injections given without embolus. Massed statistics give 0.0024% mortality from that cause. Embolism probably in regions remote from the injection, as a result of inactive venous circulation. Ambulant treatment advised, wherever possible, but if rest in bed necessary, movement of limbs should be carried out frequently and patient encouraged to sit up.—F. Remenovsky, per *Brit. med. J. Epit.*, i/1934, 27.

Strong solutions of dextrose (50%) and salt (30%) have gone out of favour and are only occasionally used in allergic cases.—A. Dickson Wright, *Brit. med. J.*, i/1940, 665.

**VOMITING OF PREGNANCY.** Glucose intravenously 5 to 10%, 4000 ml. in 24 hours.—*Brit. med. J. Epit.*, ii/1930, 64.

Intravenous injections of 50 to 75 g. of dextrose in 200 to 300 ml. distilled water (25% solution) used. The addition to the injection of 1 unit of insulin to 5 to 10 g. of dextrose did not seem to have any clinical advantages. Vomiting

usually ceased in 12 to 24 hours.—P. Titus, *J. Amer. med. Ass.*, ii/1925, 491. W. Thalhimer gives 100 g. of dextrose intravenously in as much water as the condition of the patient indicates (1 or 2 litres), the injection taking from 3 to 5 hours, and administers *hypodermically* 1 unit of insulin for every 3 g. of dextrose. Vomiting usually ceased in 6 to 8 hours.—*Ibid.*, 493.

**Ampulla Dextrosi (L.C.C.).** (a) Dextrose 5%, sterilised water to 500 ml.; (b) dextrose 50%, sterilised water to 10 or 50 ml.

**Enema Dextrosi (B.P.C.).** *Dose.*—4 ounces (120 ml.). 10% w/v in water or peptonised milk.

**Enema Dextrosi (St. M.H.).** Dextrose 1 oz., sodium chloride 1 dr., water to 1 pint.

**Liquor Dextrosi et Sodii Chloridi (B.P.C.).** *Syn.* GLUCOSE-SALINE SOLUTION.

A sterile solution containing 5% w/v of dextrose and 0.9% of sodium chloride. Although hypertonic when first injected, the rapid absorption of the dextrose renders the resulting solution isotonic.

**Modified Glucose-Saline Solution.** Dextrose 250 g., acacia 50 g., magnesium sulphate 1 g., sodium bicarbonate 16.5 g., sodium chloride 30 g., potassium dihydrogen phosphate 0.9 g., potassium sulphate 1.75 g., water to 5000 ml. Dissolve the acacia in 50 ml. of water, strain, and autoclave at 110°. Allow to stand if possible for 24 hours. Filter through Gooch asbestos on a sintered glass filter, dissolve the dextrose and the salts except the sodium bicarbonate, make up to 1000 ml., sterilise, allow to stand, filter, and again sterilise. Dissolve the sodium bicarbonate in 4000 ml. of water, add the saline solution, filter, distribute into flasks, displace the air by carbon dioxide, close the flasks with rubber bungs, tied down, and again autoclave. Has been administered in amounts of up to 20 pints in 4 days without causing rigor.—E. Lloyd, *Pharm. J.*, i/1936, 399.

**WOUND SHOCK.** The danger of intravenous administration of glucose saline in cases of shock, when the plasma proteins have been depleted by hæmorrhage or local plasma loss, is due to the fact that the normal amount of water cannot be retained in the circulation. Hence, there is a risk of pulmonary oedema. The intravenous administration should be preceded by a transfusion of whole blood or plasma. A pint of 5% glucose should be given, mixed or alternated, with every pint of saline. The rate of administration should be slow—a drip infusion at the rate of 40 drops to the minute is suitable for the average case. If dehydration is severe the rate must be increased.—“The Treatment of Wound Shock,” M.R.C. War Memo. No. 1, H.M.S.O., 1941.

**Soluté Injectable Hypertonique de Glucose (Fr. Cx.).** Glucose 300 g., distilled water to 1000 ml.

**Soluté Injectable Isotonique de Glucose (Fr. Cx.)** is 5% isotonic solution, sterilised at 110° in neutral glass.

**Cabiven (Coates & Cooper, London).** A 66% solution of grape sugar for injection in varicose veins. Issued in ampoules of 5 and 10 ml.

**Decrose (Boots, Nottingham).** Preparation of dextrose, calcium glycerophosphate and vitamin D. For use wherever dextrose is required, and especially in expectant and nursing mothers and growing children.

**Dextrose-C (British Drug Houses, London).** A preparation of medicinal dextrose containing 100 i.u. of vitamin C in each 100 grains. For use in debilitated or pyrexial conditions and in the vomiting of pregnancy.

**Glucodin (Glaxo Laboratories, London).** 98% medicinal glucose with 4½ gr. of calcium glycerophosphate and 250 i.u. of vitamin D (calciferol) in each ounce. Especially indicated in conditions associated with ketosis in which glucose therapy is applied to patients who must subsist for long periods on a low fat diet.

**Glucose B-D (Crookes Laboratories, London).** Each teaspoonful contains 75 i.u. of vitamin D and 75 i.u. of vitamin B<sub>1</sub>. *Dose.*—1 to 2 teaspoonfuls three times daily.

**Glucosum Liquidum (B.P.).** *Syn.* CORN SYRUP, GLUCOSUM (U.S.P. XI). Consists of a mixture of dextrose, maltose, dextrin and water, and occurs as a viscous mass containing about 20% of water. Sp. gr. about 1.6. It is prepared by the hydrolysis of starch.

**Enema Glucosi Liquidii** (B.P.C.). Dose.—4 ounces (120 ml.). 10% w/v in water or peptonised milk.

**Pigmentum Glucosi** (T.H.). Glucose 25, glycerin to 100. For ozaena.

**Syrupus Glucosi Liquidii** (B.P.). Liquid glucose 33.3% w/w with syrup. Used as a pill excipient.

**Dextrin** (P. *Helv. V, Fr. Cx., P. Jap. V*). Syn. BRITISH GUM. In yellowish powder or gum-like masses. Is obtained commercially by heating starch, which has been moistened with dilute nitric acid and dried, at 110° to 115°. Consists principally (there are various other dextrins formed before this) of achroodextrin which is the ultimate product of starch hydrolysis before the grape sugar stage is reached. It is soluble in water, alcohol 60%, and ether.

**Dextrin-Maltose** (Allen & Hanburys, London). A starch-free mixture of carbohydrates issued in six forms. No. 1 contains sodium chloride 2%, No. 2 is salt-free, No. 3 contains potassium bicarbonate 3%, No. 4 vitamin D, No. 5 sodium chloride 2%, and iron 20 p.p.m., and No. 6 vitamin C.

**Lactosum** (B.P., *Fr. Cx., P. Helv. V, P. Dan.*).

Syn. SACCHARUM LACTIS (P. *Jap. V*), MILK SUGAR.

$C_{12}H_{22}O_{11} \cdot H_2O = 360.2$ .

Dose.—*ad lib.*

Lactose is a disaccharide, obtained by evaporating the whey of milk to a low bulk and allowing to crystallise. It occurs as a white crystalline powder, odourless and slightly sweet. It is dextro-rotatory and reduces Fehling's solution. Lactose exists in two modifications corresponding to the  $\alpha$  and  $\beta$  isomerides. The milk sugar of commerce is  $\alpha$ -lactose.  $\beta$ -lactose is also obtainable. It is anhydrous, more soluble than  $\alpha$ -lactose, and passes into the latter form in solution.

**Soluble** 1 in 7 of water; almost insoluble in alcohol 90%, chloroform and ether.

Used in humanising cows' milk for infant feeding. Is diuretic and laxative in large doses. It is said to be a useful addition to magnesia as a laxative; it increases the solubility of the latter by combination.

A dose of  $\frac{1}{2}$  to 1 oz. in the morning in a large cup of weak tea a useful laxative. Of value in flatulence and spasm of the colon.—T. C. Hunt, *Lancet*, ii/1931, 872.

**Lævulosum** (B.P.). Syn. DIABETIN, FRUCTOSE.

$C_6H_{12}O_6 = 180.1$ .

A monosaccharide obtained from "invert sugar" and occurring as a whitish, crystalline, hygroscopic powder, reducing Fehling's solution. It is lævorotatory.

A stronger sweetening agent than cane sugar; it has a pleasant flavour. Specially suitable for diabetics. Since lævulose does not raise the concentration of sugar in the blood, except where there is hepatic derangement, it is employed as a test for liver efficiency (see Vol. II).

Very **soluble** in water, less soluble in alcohol 90%; insoluble in dehydrated alcohol or ether.

**Sorbitol**. Syn. and Prop. Name. d-SORBITE, SIONON (Bayer Products, London).  $C_6H_8(OH)_6 = 182.2$ .

d-Sorbitol, a sugar occurring in apples, pears, etc., and usually obtained from cerelese (a crystalline form of glucose) by treating with hydrogen under pressure. It crystallises with  $\frac{1}{2}$  to 1  $H_2O$  as

colourless or white, sweet crystals, which do not reduce Fehling's solution.

**Soluble** in water and hot alcohol.

**Uses.** Sorbitol is used as a substitute for glycerin, to which it is chemically and physically akin, in tooth pastes; its use has also been suggested as a glycerin substitute in pharmaceutical preparations. In diabetes it is used in a daily dose of from 30 to 80 g. as a sweetening agent in place of sucrose, since it does not produce a rise in blood sugar.

Can safely be used as a substitute for sugar in diabetes, but the probability of intestinal irritation must limit the dose. Also its price makes it a luxury which can usually be more economically provided by the use of ordinary sugars and slightly more insulin.—W. W. Payne, R. D. Lawrence and R. A. McCance, *Lancet*, ii/1933, 1258.

Up to 30 to 80 g. daily may be given to diabetics with other foods.—*Per Prescriber*, 1929, 419. Can be metabolised more easily than glucose. Quantities up to 3 ounces a day rarely produce diarrhoea.—*Brit. med. J.*, ii/1930, 105.

**Manna** (B.P.C., U.S.P. XI, *Fr. Cx.*, *P. Helv. V*, *P. Dan.*).

**Dose.**— $\frac{1}{4}$  to 4 drachms (2 to 16 g.), or more.

A saccharine exudation from *Fraxinus Ornus* (Oleaceæ). In flattish, somewhat three-edged pieces. Contains 40 to 60% of mannitol (*syn.* mannite, *P. Ital. V*, *P. Ned. V*),  $C_6H_8(OH)_6$  = 182.1, a non-fermentable sugar, which does not reduce Fehling's solution, and other sugars. Has mild laxative properties.

**Mel Depuratum** (B.P.). *Syn.* CLARIFIED HONEY, MEL DESPUMATUM, MIEL BLANC (*Fr. Cx.*)

**Dose.**— $\frac{1}{4}$  to 2 drachms (2 to 8 g.).

Prepared by melting honey, allowing to stand, straining off the scum rising to the surface and adjusting the sp. gr. to 1.36 by adding water.

**Aqua Mellis** (B.P.C.). HONEY WATER.

Oils of bergamot, lavender, clove and sandal wood, musk and saffron with triple rose water, triple orange-flower water, honey and alcohol 90%.

**Oxymel** (B.P.). **Dose.**— $\frac{1}{4}$  to 2 drachms (2 to 8 ml.). Acetic acid 15, distilled water 15, purified honey to 100.

**Sucrosom** (B.P., U.S.P. XI, *Fr. Cx.*, *P. Helv. V*, *P. Dan.*).

*Syn.* SACCHARUM PURIFICATUM, SACCHAROSE, SUCROSE.

$C_{12}H_{22}O_{11}$  = 342.2.

In crystals or white powder.

In addition to the sugar obtained from the juice of the sugar cane, *Saccharum officinarum* (Gramineæ), various grades of granular cane and beet sugar, both with and without the addition of "blue," are marketed. For the manufacture of syrups a sugar without the colouring matter is essential. B.P., *Fr. Cx.* and U.S.P. XI allow also beet sugar from *Beta vulgaris* var. *Rapa* (Chenopodiaceæ).

**Soluble** readily 2 in 1 of water, 1 in 60 of alcohol 90%.

**Uses.** Is used for the same purposes as dextrose, but is not so readily assimilated since it has to be broken down in the body to dextrose before it can be stored as glycogen in the liver. It has been given intravenously as strong as a 50% solution, but an



isotonic solution (920·6 grains per pint, i.e., 10·5%) would appear preferable. It is added to infants' foods made of dried milk.

**RELATIVE SWEETNESS OF SUGARS.** If the sweetness of sucrose is rated as 100, lævulose deserves a value of 173, dextrose 74, maltose 32, galactose 32, and lactose 16.

**Solution for injection:** Sucrose 500 g., citric acid 0·1 g., sodium phosphate 3·65 g., water to 1000 g. The solution is prepared aseptically and heated for one hour at 100°. It may be used in place of dextrose.—K. K. Jespersen, *Dansk Tidsskr. Farm.*, 1940, 14, 27.

Intravenous injections of 100 ml. of 50% sucrose solution are of value for reducing intracranial pressure in cases of acute brain injury, and are preferable to dextrose injections. The injections are without untoward effects.—E. V. Hahn, F. B. Ramsey and K. G. Kohlstedt, *J. Amer. med. Ass.*, 1/1937, 773.

**Saccharum Ustum.** Caramel is prepared by heating sucrose at 180° to 200° to form a thick black mass which is diluted with hot water to a sp. gr. of 1·4.

**Liquor Sacchari Usti (B.P.C.)** is a mixture of equal volumes of burnt sugar and chloroform water.

### **Syrupus (B.P.).**

Sucrose 667, water to 1000 by weight. Sp. gr. not less than 1·32. 9 fl. oz. of syrup contain approx. 8 oz. of sucrose. *U.S.P. XI* orders sucrose 85, water *q.s.* to measure 100. Weaker strengths of syrup do not keep well. Potassium carbonate 1 grain in 12 ounces of syrup has been found to prevent crystallisation. Best temperature for producing syrup free from invert sugar is thought to be 90°. Syrupus Simplex (*Fr. Cx.*) is either "heat-prepared" (165 g. of sucrose to 100 g. of water), or "cold-prepared" (180 g. to 100 g. of water).

The Addendum (War Emergency Formula) 1917 to the *B.P.C.* 1911, included Syrup Substitute (*syn.* SYRUPUS FACTITIUS, ARTIFICIAL SYRUP) made by mixing tragacanth powder 0·7, with chloroform 0·5, adding water 90, shaking till uniformly diffused and adjusting to 100 with water.

**Invert Sugar** is prepared by action of dilute mineral acid on sucrose. It consists of a mixture of equal weights of dextrose and lævulose. A useful substitute for cane sugar in dyspepsia—more easily borne in gastritis.

Invert sugar forms in simple syrup on keeping—that made by cold process produces more than hot. In 18 months it may reach 6%.

Solutions of invert sugar have been used in the injection treatment of varicose veins. They are claimed to have the advantage of not causing cramp or sloughing if accidentally injected outside the vein. From 5 to 20 ml. of a solution containing from 60 to 75 g. of invert sugar in 100 ml. is given.

### **Invert Sugar Solution for Injection Treatment of Varicose Veins.**

760 g. of sucrose is dissolved in water, 1 ml. of N/1 hydrochloric acid is added and the solution made up to a litre. After filtering, the solution is filled into 5·5 ml. ampoules which are sterilised at 120° for thirty minutes, inversion occurring simultaneously. This product has a pH of 3, but this is of no importance since the solution has no buffering action.—S. Hansen, S. A. Schon and G. Tonnesen, *Dansk Tidsskr. Farm.*, 1933, 7, 26.

**Theriaca, syn. TREACLE**, is the uncrystallisable residue from sugar-refining. A 50% solution in hot milk in doses of 5 to 20 ounces is used as an enema.

**DIGITALIS FOLIUM***B.P., U.S.P. XI, Fr. Cx., P. Jap. V.**Syn. DIGITALIS, FOXGLOVE LEAF.*

[P1] "*Digitalis*, glycosides of; other active principles of *digitalis*."

[81] "*Digitalis*, glycosides and other active principles of, except substances containing less than one unit of activity (as defined in the 'British Pharmacopœia') in two grammes of the substance."

[86] "*Digitalis*, glycosides of; other active principles of *digitalis*—specify proportion as the number of units of activity as defined in the 'British Pharmacopœia' contained in a specified quantity of the preparation."

The leaf of *Digitalis purpurea* (Scrophulariaceæ) rapidly dried at a temperature of 55° to 60° as soon as possible after collection. *I.A.* requires the powdered entire second-year leaf; adopted by *Fr. Cx.* and *P. Belg. IV*; *P. Ned. V* specifies drying at 55° to 60°. *P. Helv. V* collects when dry, and dries immediately at 40° and then at 55° to 60° for  $\frac{1}{2}$  hour.

**Incompatible** with preparations of cinchona and with lead acetate, also with iron salts (but the blackening is preventable by citric acid) and with iodine and potassium iodide.

**Cumulative Action.** The average rate of elimination is 25 m. of tincture, or about 2 gr. of standardised leaf per day, but it may be substantially more or less than this. Signs of toxic action are anorexia, nausea, headache and diarrhœa (nausea may be due to cardiac failure and not to digitalis), followed by runs of extrasystoles or ventricular tachycardia. Administration should be stopped for 24 hours, and smaller doses given afterwards.

The more common symptoms of overdosage, such as anorexia, nausea, vomiting, and diarrhœa are quite generally known. Less common phenomena justify re-emphasis. Coupled beats and the development of partial or complete heart block demand immediate discontinuation of the drug.

The toxic effects of digitalis on the brain and certain nerve tissues are not sufficiently appreciated although their importance is outstanding and they have been known to result in death. Prominent among these symptoms are disturbances in vision, consisting of dimness of vision, inability to focus the eyes, difficulty in the identification of objects, the presence of scotoma and diplopia, and yellow and green vision. The last are striking symptoms and are often alarming evidence of digitalis poisoning. Prodromal symptoms frequently occur and if properly interpreted, so that the administration of the drug is discontinued, the more prominent and serious disturbances may be avoided. They consist of restlessness, increased nervous irritability, and periods of disorientation regarding time and place. If stupor supervenes, death usually ensues. It is important to realise the fact that the cerebral manifestations of digitalis intoxication may occur independently of nausea, vomiting, and so forth. Occasionally, paroxysms of tachycardia occur; they usually arise in the ventricles, and have been known to result in death.—F. A. Willius, *Proc. Mayo Clin.*, 1935, 579.

The rule as to the proper dosage of digitalis in use at the Mayo Clinic, and which in most instances works satisfactorily, is to give one-tenth of the patient's bodyweight (measured in pounds) in grains or cat units of digitalis. This usually is sufficient to digitalize the patient when administered over three or four days. Digitalis intoxication is more likely to occur in the old arteriosclerotic person than in any other type of individual.—H. L. Smith, *Proc. Mayo Clin.*, 1938, 574.

**Antidotes.** Empty stomach by emetic or by stomach tube, using dilute tannic acid solution. Keep patient lying down and

warm. Give stimulants, e.g., brandy,  $\frac{1}{2}$  oz., or aromatic spirit of ammonia,  $\frac{1}{2}$  dr., in water. Atropine,  $\frac{1}{100}$  gr., hypodermically. Chloral hydrate, 20 gr., may be necessary. Chloroform inhalations. Amyl nitrite has been recommended.

**Uses.** Digitalis is used in medicine for three purposes: (1) as a stimulant in acute circulatory failure, (2) as a diuretic, and (3) as a cardiac tonic in chronic heart disease; of these the most important and the most widely employed is the last-mentioned.

Digitalis has a narrowing influence upon the arteries. Acting on the vagus, it pulls the reins of the heart. Acting on the heart muscle, it is a most useful whip, at the same time providing it with food by improving the circulation. Slowing the heart, it makes it regular also. This slowing gives the heart an opportunity of resting, so secondarily improving contractility, conductivity and excitability. By primary action it increases its strength, regulating its rhythm by depressing excitability and conductivity. In large doses it may increase excitability, causing extra-systoles, perhaps diminish contractility and, by causing long pauses, do harm to the circulation. All these influences vary according to dose, form in which it is given and the conditions of the heart.

The most remarkable therapeutic effect of digitalis is seen in *auricular fibrillation*; in this it is almost specific, causing a rapid diminution in the number of ventricular beats, rendering the heart's action more efficient and improving the circulation.

In *auricular flutter* it has the peculiar effect of changing the flutter to fibrillation, but when the drug is withdrawn the heart changes back, not to flutter, but to normal rhythm.

In *partial heart block* it exaggerates the condition and should in general be avoided, though by tending to quicken the beat it may be of some value in *complete heart block*.

Digitalis has practically no effect in reducing the rapid pulse of fevers, and although it has been widely employed in *pneumonia*, its routine use in this condition has been deprecated by most workers.

Apart from the foregoing, digitalis is employed with advantage in a large number of conditions in which the efficiency of the heart is impaired and there is deficient circulation.

The only cases likely to show bad effects are those with damaged auriculo-ventricular bundle, in whom heart-block may result. Raised blood pressure is no contraindication to the use of digitalis, and is often due to some secondary effect of the heart failure.

When used as a diuretic the kidneys must be capable of responding to its action, which is exerted by increasing the force of the cardiac systole and forcing more blood through the organs.

Apart from its well-established indications in which the drug may be expected to produce results of value, it is still common to find it prescribed in various states in which it can be of no real benefit and may even be harmful. Thus, the routine use of digitalis increases the mortality in lobar pneumonia, is believed to increase the post-operative death rate in thyrotoxicosis, and handicaps recovery in the peripheral circulatory failure of shock and collapse.—R. Gilchrist, *Practitioner*, ii/1939, 436.

Congestive failure provides the main indication for the administration of digitalis. Its influence removes the signs and symptoms caused by congestive failure, and if such symptoms are absent little is gained by its use. Tachycardia in itself (unless due to auricular flutter) is seldom an indication for digitalis; nor is bradycardia a contraindication. It should not, therefore, be a routine measure in hyperthyroidism, pneumonia or shock. The slowing of the pulse is not the best guide to the effectiveness or otherwise of digitalis; the improvement in the patient's symptoms and sense of well-being is often more reliable.—A. R. Gilchrist, *Edinb. med. J.*, 1939, 46, 233.

**AURICULAR FIBRILLATION.** 54 cases of auricular fibrillation treated with 0·1 ml. of tincture per lb. weight, with sodium bicarbonate, aromatic spirit of ammonia, and chloroform water to 3 ounces. The average dose was 13 ml.; the average pulse before use was 140 and 8 hours after it was 91. Toxic effects occurred once and vomiting twice, and the average duration of good effect was 6 days, so that small doses were needed at the end of a week. The method is a measure of urgency only.—G. J. Langley, *Brit. med. J.*, i/1927, 1043, 1162.

**CONGESTIVE HEART FAILURE.** Rest and digitalis the outstanding methods of treatment. *Digitalisation.*—Calculate dose in minims by multiplying body-weight in pounds by 2½, i.e., a 10-stone patient requires 350 minims. (Initially it is best to give ½ of this dose.) In urgent cases if no strophanthus or digitalis has been given previously, safest to give half the dose at once, ½ the dose after 6 hours, ½ after a further 6 hours, and a further ½ after 6 hours. Often not sufficient urgency to warrant more than 90 minim doses three or four times daily.—Maurice Campbell, *Practitioner*, 1931, 32.

**PNEUMONIA.** The infusion of digitalis helps the heart to resist depressant action which the pneumonia toxin has. 1 dr. of the infusion every 4 hours, increasing to ½ oz. every 4 hours, or 3 hours, night and day. Begin about second or third day.—E. M. Brockbank, *Brit. med. J.*, i/1930, 974.

From a study of 1000 cases of lobar pneumonia no evidence was found that the routine use of digitalis was useful. When auricular fibrillation (in about 5% of cases) is present digitalis may save life, though patients frequently recover without it, but routine digitalis therapy in lobar pneumonia is dangerous.—H. Gold and co-workers, *Amer. J. med. Sci.*, April, 1933, 509.

Digitalis does not appear advisable in pneumonia, except for patients with definite auricular fibrillation.—Sollmann, 5th Edn., 1936.

[P1-81] **Acetum Digitalis (P. Ned. IV).** Digitalis leaves 1, dilute acetic acid (6%) 9, alcohol (90%) 1. Macerate 5 days.

[P1-81] **Digitalis Pulverata (B.P. Add. I).**

*Dose.*—½ to 1½ grains (0·03 to 0·1 g.); single doses, 3 to 10 grains (0·2 to 0·6 g.).

Digitalis leaf reduced to powder, no part being rejected, and adjusted by admixture with exhausted leaf or with weaker leaf to contain 10 units per gramme.

For preparing the fresh infusion and the tincture, biologically standardised but unadjusted leaf is also recognised by the B.P.

The therapeutic efficiency of a number of cardiotonics has recently been determined by comparative tests on patients with heart disease. The following are arranged in order of efficiency: powdered digitalis leaf, digitaline (digitoxin), Digifoline, Digoxin, tincture of digitalis, Folinerin, ouabain and strophanthin. The three latter were shown to give results inferior to those of digitalis or its preparations.—F. Prescott, *Chem. & Drugg.*, i/1940, 251.

From a six-year study of the clinical efficacy of digitalis preparations it was concluded that there was no evidence that the glucoside preparations (Digalen, Verodigan, Nativelle's Digitaline, and Digoxin), when given by mouth, were quicker in action, more efficient, more prolonged in action or less toxic than standardised whole digitalis leaves.—W. D. Stroud and J. B. V. Veer, *J. Amer. med. Ass.*, ii/1937, 1808.

[P1-81] **Digitalis Pulverata (U.S.P. XI).**

*Average Dose.*—1½ gr. (0·1 g.).

Standardised dried and powdered leaf; 0.1 g. is equivalent to 1 to 1.1 U.S.P. digitalis units (which are identical with the international units).

**Suppositories.** The following formula is suggested for suppositories containing the active principles in the aqueous phase of an oil-in-water emulsion, thus facilitating absorption. 1.1 g. of powdered digitalis is infused with 9 ml. of hot water and the cooled liquid is emulsified with 15 g. of cocoa butter containing 1% of ovolecithin and made into 10 suppositories. The addition of 1% of Nipagin-Nipazol combination as a preservative is suggested.—H. Eschenbrenner, *Pharm. Ztg., Berl.*, 1936, 1170.

[P1-S1] **Tabellæ Digitalis Pulveratæ (B.P.C.)** contain 1 gr. (0.06 g.).

[P1-S1] **Extractum Digitalis Stabilisatæ (Fr. Cx.)**. Dried leaves extracted with 70% alcohol, evaporated to soft extract.

[P1] **Infusum Digitalis Recens (B.P.)**.

*Dose.*—90 to 300 minims (6 to 20 ml.); single dose, 1 to 4 oz. (30 to 120 ml.).

Prepared from the equivalent of 0.5% of international standard digitalis powder. A concentrated infusion must not be used; when Infusum Digitalis is prescribed the fresh infusion is to be dispensed.

This is an active preparation. In use it may well be combined with some vasodilator.

The infusion has such practical disadvantages that its use should now be abandoned.—C. Hoyle and J. W. Linnell, *Practitioner*, i/1936, 94.

[P1-S1] **Liquor Digitalis ad usum internum (P. Ned. V).** *Syn.* DIGISOL.

*Dose.*—Maximum single 3 ml.; maximum daily 10 ml.

Similar to the solution for injection following except that, after the evaporation of the chloroform, the volume of water used to extract the residue is 88% of that of the chloroform. Finally to every 88 parts of this solution are added 12 parts of 96% alcohol.

[P1-S1] **Liquor Digitalis ad Injectionem (P. Ned. V).** *Syn.* DIGISOL FOR INJECTION. *Dose.*—5 ml. maximum single and *per diem*.

Macerate one part of powdered digitalis leaves with 8 parts of water during 48 hours at a temperature not exceeding 15°, strain and filter. Shake the filtrate with an equal volume of chloroform during 48 hours, avoiding emulsification. Reserve the chloroform solution and evaporate a measured volume of the aqueous layer on the water bath to a thick extract. To this add sufficient exsiccated sodium sulphate to form a dry powder. Shake this during 24 hours with a volume of the chloroformic extract equal to that of the evaporated aqueous solution and filter. Measure the volume of the chloroform and distil off. Treat the residue with water equal in volume to that of the chloroform, using small quantities at a time; dissolve 0.8% of sterile sodium chloride in the solution and filter. Sterilise by heating on 3 consecutive days for 1 hour at 70° to 80°. *Keep in a cool place away from light.*

A lethal dose for a cat of 2 ml. per kg. body weight is required by *P. Ned. V.* The preparation is considered to be too dilute for injection when rapid digitalisation is required.

[P1] **Mist. Digital. et Caffein. (N.I.F.)**.

Caffeine 1 gr., tincture of digitalis 7½ m., solution of strychnine hydrochloride 3 m., concentrated infusion of orange 15 m., water to ½ oz.

[P1] **Mist. Digital. c. Scill. (N.I.F.)**.

Tincture of digitalis 5 m., tincture of squill 10 m., potassium acetate 10 gr., chloroform water to ½ oz.

[P1-S1] **Pilulæ Digitalis Compositæ (B.P.C.)**.

*Syn.* GUY'S PILL, ADDISON'S PILL, BAILLIE'S PILL, PILULÆ DIGITALIS CUM SCILLA.

*Dose.*—1, as often as 3 times a day.

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Mercurial pill 1, powdered digitalis 1, squill 1. In grains for one pill; in grammes for fifteen. Used in cardiac dropsy.

[D-P1-81] **Niemeyer's Pill.** *Syn.* HEIM'S PILL.

*Dose.*—1 pill thrice daily.

Powdered digitalis  $\frac{1}{2}$  gr., ipecacuanha  $\frac{1}{2}$  gr., powdered opium  $\frac{1}{2}$  gr., extract of helenium  $\frac{1}{2}$  gr.

Used in combating the fever of phthisis. When the fever is of the periodical type, one grain of quinine sulphate is added to the above formula.

The B.P.C. gives Niemeyer's Pill as a synonym for Pilulæ Digitalis Co. Whitla gives the formula—digitalis  $\frac{1}{2}$  gr., quinine 1 gr., opium  $\frac{1}{2}$  gr., Heim's pill being similar with ipecacuanha  $\frac{1}{2}$  gr. in place of the quinine. In "Lectures on Phthisis" Niemeyer gives the formula of Heim's pill as above, with or without quinine, and says that "it has become a very common pill at my clinic."

For preparations of similar composition which are *exempt* [D] see pp. 1139 and 1140.

[P1-81] **Tabella Digitalis et Hydrargyri Composita** (*St. B. H.*). *Syn.* GUY'S PILLS (*St. G. H.*).

Powdered digitalis, mercury pill and squill, of each 1 gr.

[P1-81] **Tinctura Digitalis.** (*B.P., Fr. Cx., F.E. VIII, P. Belg. IV, and P. Ital. V.*)

*Dose.*—5 to 15 minims (0.3 to 1 ml.); single dose, 30 to 90 minims (2 to 6 ml.).

Frequently single doses of as much as  $1\frac{1}{2}$  drachms are given. Large single doses in many cases preferable to repeated small doses.

May be prepared from unstandardised leaf, the tincture being subsequently biologically assayed, or it may be prepared from standardised leaf, using a quantity equivalent to 1000 units (80 g. of international standard powder) per litre, by percolation with alcohol 70%. *B.P. Add. I* permits also, as a further alternative, maceration for two days with alcohol 70% in place of percolation. It is required to contain 1 unit per ml.

[P1-81] **Tinctura Digitalis** (*U.S.P. XI*).

*Average dose.*—15 minims (1 ml.).

Powdered digitalis leaf, 1 in 10, biologically standardised and adjusted so that 1 ml. is equivalent to 1 to 1.1 U.S.P. digitalis units.

**Stability of the Tincture.** Experiments extending over three years indicate that the addition of glacial acetic acid and sodium acetate to a tincture prepared from the de-fatted drug yields a stable preparation.—L. W. Rowe and W. L. Scoville, *J. Amer. pharm. Ass.*, 1933, 1087.

In tropical climates such as that of India, tincture of digitalis undergoes deterioration in a short time. Tinctures become darkish in colour on dilution and are evidently considerably weaker in therapeutic efficacy. Dosage used in India far too small.—R. N. Chopra, S. C. Bose and P. De, *Indian med. Gaz.*, Mar., 1925, 97.

In cold countries the average quantity of tincture of digitalis required to cause toxic effects varies from 4 to 7 dr., but in Calcutta the smallest dose required was 9 dr. and the highest 29 dr., while the average was well over 14 dr. Due to loss of potency of tincture and increased decomposition in the alimentary tract and liver. Toxic effects with B.P. tincture in 15 m. doses thrice daily very rare in India. To obtain prompt results in grave cases, 2 to 3 dr. per day for 5 days should be given.—S. C. Bose, *Indian med. Gaz.*, Apr., 1925, 154.

[P1-81] **Digitalinum (B.P.C.).** *Syn.* DIGITALINUM PURUM GERMANICUM.

*Dose* (by subcutaneous injection).—For a single administration  $\frac{1}{2}$  to 1 grain (0.03 to 0.06 g.); for repeated administration  $\frac{1}{5}$  to  $\frac{1}{2}$  grain (0.004 to 0.012 g.).

A mixture of glycosides from the seeds of *Digitalis purpurea* (Scrophulariaceæ) standardised biologically to contain 80 units of activity (equivalent to 8 g. of the international standard powder) per gramme. It occurs as an odourless, yellowish-white powder with an intensely bitter taste and contains digitalinum verum,  $C_{36}H_{56}O_{14}$ , a definite physiologically-active glycoside, together with a large proportion of water-soluble glycosides of which little is known and the physiologically-inactive glycosides digitonin,  $C_{55}H_{90}O_{29}$ , and gitonin,  $C_{49}H_{80}O_{28}$ .

*Soluble* readily in water and alcohol; sparingly soluble in chloroform and ether.

*Caution.* When digitalin is ordered (with the relative *bold dose*) Digitalinum (B.P.C.) should be given. DIGITALINE (*Fr. Cx.*) consists almost entirely of digitoxin, and the dose is much smaller, *v.* Digitoxinum.

[P1-81] **Injectio Digitalini (B.P.C.).**

*Dose* (by subcutaneous injection).—For a single administration, 15 to 30 minims (1 to 2 ml.); for repeated administration, 3 to 6 minims (0.2 to 0.4 ml.). Contains per ml. 0.03 g. of digitalin, equivalent to about  $2\frac{1}{2}$  units of activity.

*Indications for hypodermic use.*—

The hypodermic method alone is admissible (1) in grave cases where cardiac failure is imminent and immediate and certain action is required, because in such cases gastro-intestinal absorption is slow and uncertain, (2) In cases in which it is desirable to safeguard the stomach and to avoid setting up gastric intolerance or embarrassment of cardiac action by a dilated stomach, the hypodermic method must be used, *e.g.*, in typhoid with failing heart, where diuresis is essential; in vomiting in arteriosclerotics, where the stomach becomes distended on the slightest irritation.

[P1-81] **Nativelle's Crystallised Digitaline (Laboratory Nativelle, London)** is probably identical with digitoxin, *q.v.*;  $\frac{1}{10}$  mg. ( $\frac{1}{1000}$  grain) contains one unit of activity. It is supplied in the following forms: pink granules of  $\frac{1}{10}$  mg. ( $\frac{1}{1000}$  gr.) and white granules of  $\frac{1}{2}$  mg. ( $\frac{1}{2000}$  gr.); 1 in 1000 solution, 5 drops correspond to  $\frac{1}{10}$  mg. ( $\frac{1}{1000}$  gr.); ampoules for intramuscular injection, 1 ml. =  $\frac{1}{2}$  mg. ( $\frac{1}{2000}$  gr.). *Dose.*—(1) *small dose:*  $\frac{1}{10}$  mg. or 5 drops of the 1 in 1000 solution daily for the first 5 days of every 10 or 15-day period, continued indefinitely if necessary; (2) *medium dose:* 2 granules of  $\frac{1}{10}$  mg. or 10 drops of the 1 in 1000 solution daily for 5 days, then cease for a week and repeat, or replace by the small dose; (3) *strong dose:* intensity of treatment depends upon the case, administration being pushed to saturation point as evinced by a pulse of 60; the patient should be examined daily and treatment stopped if signs of intoxication appear; the threshold is usually reached with 2 to 3 mg. given over a period of 10 days. The intravenous or intramuscular injections are reserved for cases of intolerance to the medicament *per os*, or for cases of urgency.

Digitalis leaf was compared with Digitaline Nativelle in a selected group of 49 patients in a series of experiments extending over periods of 24 to 54 weeks. Digitaline Nativelle is about 200 times as potent as digitalis by cat and frog methods, but 1800 times as potent when the two are compared in man (method of assay in man described). It requires from 6 to 12 cat units of digitalis leaf to produce the effects of 1 cat unit of Digitaline Nativelle, and full digitalisation is accomplished by a total of 3 cat units by the mouth, compared with 25 cat units of digitalis.—H. Gold *et al.*, *J. Pharmacol.*, 1940, 69, 177.

**[P1-81] Tabellæ Digitalini et Nitroglycerini.**

Digitalin  $\frac{1}{10}$  gr. (0.006 g.) with glyceryl trinitrate  $\frac{1}{100}$  gr. (0.0006 g.). Useful in aortic disease. Where vascular tension is high, the addition of glyceryl trinitrate prevents increase of peripheral resistance, and thus robs the digitalis of the influence on the arterioles on account of which its administration is supposed to be contraindicated.

**[P1-81] Digitoxinum (B.P.C.). Syn. DIGITALINE (Fr. Cx.).**

*Dose.*— $\frac{1}{800}$  to  $\frac{1}{80}$  grain (0.0001 to 0.001 g.). *Caution.*—0.002 g. may be a fatal dose.

Koppe took 1 mg. of digitoxin *per os* without any certain toxic effect, but a dose of 2 mg. taken four days later nearly produced a fatal result.

Digitoxin of commerce consists chiefly of the definite glycoside digitoxin,  $C_{41}H_{64}O_{13}$ , together with a small proportion of gitoxin,  $C_{41}H_{64}O_{14}$ . *P. Belg. IV* and *F. E. VIII* have formula  $C_{34}H_{54}O_{11}$ .

It occurs as a white microcrystalline powder with an intensely bitter taste.

*Soluble* about 1 in 80 of dehydrated alcohol, and 1 in 20 of chloroform. Sparingly soluble in alcohol 90%; very soluble in more dilute alcohol. In the pure condition it is stated to be insoluble in water. There is, however, physiological and chemical evidence that it is *soluble in the presence of the other glycosides*.

Solutions may be made containing  $\frac{1}{84}$  gr. (0.001 g.) of digitoxin in 15 minims (1 ml.) of Petit's Liqueur. This quantity will approximate 40 drops, which may be considered a maximum dose. Suitable either *per os* or as an enema. May also be given in syrup—digitoxin 0.1 g., alcohol (90%) 200, distilled water 750, syrup to 2500. *Dose.*—1 to 4 drachms (4 to 15 ml.).

**[P1-81] Tablets** and **[P1-81] Granules** (Pills) of digitoxin are prepared containing  $\frac{1}{140}$  gr. ( $\frac{1}{2}$  milligramme) and  $\frac{1}{800}$  gr. ( $\frac{1}{10}$  milligramme).

**[P1-81] Poudre de Digitaline au Centième** (Fr. Cx.). Digitaline 1%, carmine 2.5%, with lactose.

**[P1-81] Soluté de Digitaline** (Fr. Cx.) contains digitaline 0.1% dissolved in alcohol (95%) 46%, glycerin 40%, and water. *Dose.*—0.3 gramme.

**[P1-81] Vin de Digitale Composé** (Fr. Cx.). 20 g. contains the equivalent of 0.1 g. of digitalis, and 1 g. of potassium acetate.

**[P1-81] Digalen** (Roche Products, Welwyn Garden City).

Stable preparations of the therapeutically active principles of digitalis leaves, pharmacologically standardised, available as oral solution, tablets, ampoules and suppositories. 1 ml. of oral solution, and each suppository, is equivalent to 0.1 g. of international standard digitalis powder (1 B.P. unit); the tablets and ampoules are each equivalent to 0.05 g. of international standard powder ( $\frac{1}{2}$  B.P. unit).

The emergency intravenous dose of Digalen, for patients who have not previously received digitalis, is 1 minim per lb. weight, i.e., one-half the full therapeutic dose. If necessary give another dose of  $\frac{1}{2}$  minim per lb. weight and repeat at 2-hourly intervals to a total of not more than 4 injections until improvement or signs of toxic action, then revert to oral use.—H. E. B. Pardee, *J. Amer. med. Ass.*, ii/1928, 147.

**[P1-81] Digifoline** (Ciba, Horsham). Total glycosides of digitalis leaf. Tablets contain  $1\frac{1}{2}$  gr. *Dose.*—As a cardiac tonic, 1 tablet for 5 days in every fortnight; as a sedative, 3 tablets during 3 days, followed by interval of 10 days; asystolic dose, 4 tablets. Also given hypodermically or intravenously (1 ml. =  $1\frac{1}{2}$  gr. standardised digitalis leaf).



[P1-81] **Digifortis** (Parke, Davis, London). Tincture of digitalis free from fat. 1.25 unit per ml. *Average dose*.—8 minims (0.5 ml.) orally two or three times a day. Also Digifortis Tablets (0.8 unit) and Capsules (0.8 unit).

[P1-81] **Digiglusin** (Lilly, London). A standardised preparation containing all the medicinally active glycosides of digitalis. Supplied as tablets each representing 0.1 g. digitalis leaf or 1 cat unit, and as ampoules containing 1 ml. of the same potency.

[P1-81] **Diginutin** (Burroughs Wellcome, London). Preparations of the total glycosides of *Digitalis purpurea* in solution or tablets, for oral administration. The solution is equivalent in strength to the B.P. tincture, 1 ml. representing 0.1 g. of international standard digitalis. Tablets represent 5 or 10 minims of the solution.

[P1-81] **Digipuratum** (Knoll, London; Savory & Moore, London). Active principles of digitalis. *Dose*.—1 tablet, 1 ampoule, or 1 ml. of liquid (each corresponding to 1½ gr. of active digitalis leaves) 3 or 4 times daily.

[P1-81] **Digitalis Exclud Suppositories** (Riddell, London). Digitalis leaf 0.1 g., caffeine 0.09 g., theophylline 0.02 g. *Dose*.—1 to 3 daily; for continuous treatment, one daily. Course of 20, then 14 days' interval and repeat. For use in the entire field of digitalis therapy, especially chronic heart complaints. No cumulative effects.

[P1-81] **Digitalone** (Parke, Davis, London). A fat-free non-alcoholic solution of the active principles of digitalis; 1 ml. = 1 i.u. Prescribed in the same dosage as Tinct. Digitalis B.P.

[P1-81] **Digitol** (Sharpe & Dohme, London). Defatted standardised tincture of digitalis.

[P1-81] **Digiveron** (Boehringer, Mannheim; Coates & Cooper, London). Gitalin component of digitalis leaves. Supplied in tablets or granules of 0.0008 g. and in suppositories containing 0.0012 g. *Dose*.—½ to 1 tablet, or 1 suppository.

[P1-81] **Digitalis Lanata** leaves contain digitoxin, gitoxin, and digoxin, each glycoside existing in the leaf in combination with dextrose and an acetyl group forming respectively the complex glycosides, digilanid A, B, and C. Digilanid C is probably identical with lanadigin. The leaf of *D. lanata* is 3 to 4 times as potent as that of *D. purpurea*, and is now used as the source for the manufacture of the crystalline glycosides.

**Chemical Relationships of Digitalis Glycosides.** According to Prof. Stoll and co-workers, from the mixed glycosides of the leaf of *Digitalis lanata*, three complex glycosides named digilanid A, B and C respectively can be separated by shaking with immiscible solvents. Digilanid A on mild alkaline hydrolysis loses an acetyl group yielding deacetyldigilanid A. Similarly digilanids B and C yield deacetyldigilanids B and C. On further hydrolysis by means of an enzyme, a molecule of dextrose is removed from each of the deacetyldigilanids, and the products obtained are respectively digitoxin, gitoxin and digoxin. The deacetyldigilanids A and B (but not C) can be separated from the mixed glycosides of *Digitalis purpurea* leaf, thus providing a connecting link between the therapeutically active principles of the leaves of the two species.

Tinctures made from *D. lanata* (Kashmir and Austrian varieties), when administered intravenously, are twice as toxic to cats as those made from the standard *D. purpurea*. *D. lanata* (Austrian) in concentrated solution produces at least 50% more slowing of the heart-beat as compared with the standard *D. purpurea*. The Kashmir variety produces the same amount of slowing of heart-beat as the standard digitalis (B.P. '32). In dilute form (1 in 20) the Kashmir variety produces much less physiological slowing of the heart as compared

with the other two. The standard *D. purpurea* is slower in action as compared with both varieties of *D. lanata*.—R. N. Chopra, J. S. Chowhan and J. C. Gupta, *Indian J. med. Res.*, 1936, Oct., 509.

[P1-S1] **Digilanid** (*Sandoz, London*). Preparations of uniform activity and composition containing the three glycosides of *Digitalis lanata* in the forms in which they occur in the leaf. It is stated to be better tolerated than other digitalis preparations and may be administered orally, intramuscularly or intravenously, the action commencing in 24 to 48 hours, 20 to 40 hours and about 10 hours respectively. Available in tablets (0.25 mg.), solution (1 ml. = 0.5 mg.) and ampoules (2 ml. and 4 ml. containing 0.4 and 0.8 mg. respectively). The adult oral dosage for general use is 1 tablet or 15 drops of solution three times daily. Parenterally, 0.8 mg. may be given once daily intravenously or 0.4 mg. twice daily intramuscularly.

[P1-S1] **Digoxin** (*Burroughs Wellcome, London*).  $C_{41}H_{64}O_{14}$ .

**Dose.**—Orally, initial dose 0.001 to 0.0015 g. ( $\frac{1}{60}$  to  $\frac{1}{40}$  grain); maintenance dose 0.00025 g. ( $\frac{1}{4000}$  gr.) twice daily. To be taken with water. Intravenous dose, 0.0005 to 0.001 g. ( $\frac{1}{2000}$  to  $\frac{1}{1000}$  grain).

A crystalline glycoside obtained from *D. lanata*, m.p. (with decomposition) about 265°.

Almost **insoluble** in water, sparingly soluble in chloroform and acetone, more soluble in dilute alcohol.

**Uses.** Is rapidly effective when given orally in auricular fibrillation, but may be given intravenously when extremely rapid effect is required. It reduces congestion in patients suffering from congestive heart failure and auricular fibrillation, and promotes diuresis when oedema is present. Orally the effect begins in 1 hour, reaching a maximum in 6 to 7 hours; intravenously the effect begins in 5 to 10 minutes and reaches a maximum in 1 to 2 hours. Available in oral solution containing 0.0005 g. per ml., in tablets of 0.00025 g., or in solution for intravenous injection containing 0.0005 g. per ml.

5 to 10 minutes after intravenous injection of 0.75 to 1.0 mg. ventricular slowing begins and is maximal in 1 to 2 hours. 1.0 mg. intravenously causes a fall in rate slightly greater than that after intravenous injection of 0.25 mg. of ouabain of 90% standard activity. Digoxin by mouth in single doses of 1.0 to 1.5 mg. causes rapid fall in ventricular rate, beginning one hour after administration and reaching full extent in 6 to 7 hours. Digoxin is absorbed and eliminated more rapidly than digitalis and causes vomiting if sufficient is given.—E. J. Wayne, per *Practitioner*, ii/1933, 314.

Since the introduction of Digoxin there is no longer much place for massive digitalisation or intravenous strophanthin in an urgent case; the former is more dangerous, the latter more likely to cause vomiting and a more difficult period of stabilisation. A dose of 1.5 mg. of Digoxin by mouth, or 1.0 mg. intravenously, is recommended in an urgent case that has not had digitalis recently, and 0.25 mg. thrice daily as an average routine dose afterwards.—M. Campbell, *Practitioner*, ii/1933, 476.

[P1-S1] **Gitoxinum**.  $C_{41}H_{64}O_{14}$ .

A glycoside present in the leaves of *D. purpurea* and *D. lanata*, m.p. (with decomposition) 285°. Similar to Digoxin in solubilities.

[P1-S1] **Cedilanid** (*Sandoz, London*). A preparation of lanatosid C, one of the three native glycosides found in *Digitalis lanata*. Available in tablets and solution for oral administration, in ampoules for intravenous injection, and in suppositories. **Dose.**—*Tablets* (0.00025 g.) 1 or 2 three times daily; *Solution*,  $\frac{1}{2}$  to  $\frac{1}{4}$  ml. (1 ml. = 0.001 g.) three times daily; *Ampoules*, 2 to 4 ml. (0.0004 to 0.0008 g.) intravenously daily; *Suppositories* (0.001 g.) 1 twice daily. Increases cardiac efficiency without influencing the heart rate to any marked degree and has a remarkable diuretic effect. Specially indicated in heart failure due to

myocardial insufficiency and that associated with disturbance of rhythm. It may be employed when other digitalis preparations present difficulties owing to toxic manifestations.

[P1-81] **Pandigal** (*Herts Pharmaceuticals, Welwyn Garden City*). Preparation of the glycoside, lanadigin, from *Digitalis lanata*. Supplied in the form of tablets, solutions, ampoules or suppositories for oral, intravenous or rectal administration in doses of 0.0002 to 0.0004 g.

**Adonis Vernalis** (*Fr. Cx., P. Austr., P. Ned. V*). Contains a hygroscopic glycoside adonidin which resembles digitalis in action. *Dose*.—In powder, 3 to 6 grains; of infusion 1 in 40, 4 drachms; of adonidin,  $\frac{1}{2}$  to  $\frac{1}{4}$  grain daily. Epilepsy has been treated with it combined with bromide. *Tincture*—leaves and stalks employed, 1 in 10. *Dose*.—10 to 30 minims. Adonidin is a local anæsthetic. In chronic glaucoma, iritis, and iridocyclitis 1% solution has been used; 3 drops relieve pain.

5 mg. of adonidin in 0.5% solution an efficient diuretic in cardiac anasarca. —*Per Yearb. Pharm.*, 1927, 218. See also *ibid.*, 1926, 237.

**Cereus (B.P.C.), syn. NIGHT-BLOOMING CEREUS, CACTUS GRANDIFLORUS**, is the fresh young shoots of *Cereus grandiflorus*. Preparations have been used as cardiac tonics free from cumulative or narcotic action, but evidence of utility is doubtful. The importation of the fresh shoots for the preparation of the small amounts of extract and tincture required is frequently inconvenient, and dried *Opuntia* flowers are sometimes used instead.

**Extractum Cerei Liquidum (B.P.C.). Syn. EXTRACTUM CACTI GRANDIFLORI LIQUIDUM.** *Dose*.—1 to 10 minims (0.06 to 0.6 ml.). 1 in 1.

**Tincturâ Cerei (B.P.C.). Syn. TINCTURA CACTI GRANDIFLORI.** *Dose*.—2 to 30 minims (0.12 to 2 ml.). 1 in 4.

**Convallaria (B.P.C., P. Helv. V). Syn. LILY OF THE VALLEY FLOWERS, MUGUET (Fr. Cx.).** The dried inflorescence of *C. majalis* (Liliaceæ). Two glycosides have been obtained from the plant: convallarin, a purgative (*dose*.—3 to 4 grains), and convallamarin (*dose*.— $\frac{1}{2}$  to 2 grains). A cardiac stimulant and diuretic. Its action is so feeble as to be almost of no value in medicine. It is an old remedy for dropsy.

**Extractum Convallariæ Liquidum (B.P.C.).** *Dose*.—5 to 10 minims (0.3 to 0.6 ml.). 1 in 1.

**Tinctura Convallariæ (B.P.C.).** *Dose*.—5 to 20 minims (0.3 to 1.2 ml.). 1 in 8.

**Cratægus Oxyacantha (N.O. Rosaceæ). Syn. ENGLISH HAWTHORN, HAW, AUBÉPINE (Fr. Cx.).**

*Dose*.—2 to 15 grains thrice daily. Liquid extract of the fruit, 10 to 15 minims. Contains a cyanogenetic glucoside. A cardiac tonic, in dyspnoea, hypertrophy, valvular insufficiency and heart oppression.

Pharmacologically there are considerable similarities between the actions of tincture of cratægus and tincture of digitalis. Clinically, however, tincture of cratægus has little effect in slowing the heart rate and does not promote diuresis. On the other hand it reduces blood pressure, and in ten cases of hypertension treated with one drachm of tincture of cratægus three times daily, there was a uniform lowering of the systolic and diastolic blood pressure. It is not cumulative and after cessation of the drug the blood pressure returns to its previous level.—J. W. P. Graham, *Brit. med. J.*, ii/1939, 951. Value in hypertension confirmed.—F. Bodman, *ibid.*, 1022.

Cratægus has a paralytant action on the respiratory centre when given intravenously, and is toxic to the heart. Chronic poisoning causes necrosis of the liver. The mammalian heart is at first slowed and strengthened, but later passes into auricular fibrillation and heart block.—J. D. P. Graham, *Quart. J. Pharm.*, 1940, 49.

**Extrait d'Aubépine (Fluide)** (*Fr. Cx.*). 1 in 1 liquid extract of the flowers with alcohol 45%.

**Teinture d'Aubépine** (*Fr. Cx.*). Prepared by macerating the bruised flowers 2 parts, for 10 days with alcohol 60% 5 parts, and filtering.

Tincture of hawthorn was made by macerating the dry powdered whole fruits with 70% alcohol for seven days. Assayed against standard tincture of digitalis it was found to possess about 14.5% of the potency of the standard preparation.—J. D. P. Graham, *Brit. med. J.*, ii/1939, 951.

**Folinerin** (*Schering, London*). Crystalline glycoside from the leaves of *Nerium oleander* in tablets containing 0.1 mg. *Dose*.—Two tablets three times daily. In all conditions in which digitalis would be given.

Has a digitalis action on pulse, diuresis and bodyweight. Is more quickly absorbed and has a shorter cumulative effect. Further clinical trial is suggested.—W. Schuler and H. Ott, *Munch. med. Wschr.*, 1937, 49.

**Verbascum Thapsus**. *Syn. MULLEIN, BOUILLON BLANC* (*Fr. Cx.*). The leaves are used as a substitute for digitalis. The flowers, together with those of *V. thapsiforme* are official in the *Fr. Cx.*

## EMULSIONES

These are usually preparations containing oil and water in which the oil is finely dispersed in the water (oil-in-water type) or, *vice versa*, in which the water is dispersed in the oil (water-in-oil type).

The latter type is not usually employed for internal administration, but chiefly as liniments, embrocations and ointments, and the following considerations apply to the oil-in-water types only. Oil-in-water emulsions are very suitable preparations for exhibiting oily substances, particularly if they are nauseous, since, being suspended in an aqueous medium, which is generally sweetened and flavoured, they do not make contact with the papillæ of the tongue. Such preparations are, moreover, readily diluted with water and aqueous preparations. In order to make the dispersion of oil more permanent, it is necessary to employ an emulsifying agent or emulgent.

### Emulgents.

The following are used for preparing emulsions for internal administration:—Acacia, decoction of chondrus (Irish moss), or yolk of egg.

**Acacia** is probably the best emulgent for this type of emulsion. When preparing an emulsion by hand, using a pestle and mortar, it is better to employ powdered acacia, but if using a machine (hand or power) it is preferable to use mucilage of acacia. In the former method, a primary concentrated emulsion should first be prepared and afterwards diluted. The following proportions are suitable for making primary emulsions:—

For fixed oils: oil 4, water 2, gum 1.

For volatile oils: oil 2, water 2, gum 1.

The powdered acacia should be added to the oil in the mortar, quickly diffused, the water immediately added and the emulsion prepared by light and quick trituration. In order to form an emulsion it is necessary that the acacia should hydrate with the

water and this may not happen if the powdered acacia is left in contact with the oil too long before adding the water. The primary emulsion should be diluted to volume with the vehicle, any salts or alcoholic liquids being added in a diluted condition just before the final adjustment to volume.

Even a good emulsion may, on standing, tend to separate into two layers, an upper concentrated emulsion and a lower very weak emulsion. This is known as "creaming." An emulsion in this condition is readily made homogeneous again by shaking, but creaming will reoccur on standing. In order to prevent creaming, either the continuous aqueous phase must be made more viscous by the incorporation of more acacia or, better still, tragacanth, or the globules of the oily disperse phase must be decreased in size. In a hand mortar-made emulsion, using the proportions of oil and gum stated above, it is almost impossible to prevent creaming if the amount of oil present is less than 20%. By employing a machine, however, the oil globules can be reduced to such a very fine size that creaming can be prevented. Acacia emulsions usually require a preservative such as chloroform (0.2%) or benzoic acid (0.6%).

**Decoction of Chondrus.** This is a cheap emulgent and can be employed to replace acacia although it does not form such a good emulsion. It is preferable to use an emulsion machine as mortar-made emulsions are usually very coarse and are prone to separate. The decoction should be freshly prepared and allowed to stand for about 18 hours before use. If a machine is used, such as a small cream machine, equal volumes of the oil and decoction should be stirred together and the mixture passed through the machine twice. A preservative such as chloroform or benzoic acid is very necessary with this type of emulsion.

**Yolk of Egg.** This is an excellent emulgent for oils. It possesses approximately double the emulsifying power of powdered acacia, volume for weight. The yolk of an egg of average size measures from 4 to 5 fluid drachms and suffices for the emulsification of 4 fluid ounces of fixed oil or 2 fluid ounces of volatile oil. White of egg is a much poorer emulgent than the yolk and it is usual to reject it, using the latter only.

The yolk should be triturated to a perfectly smooth consistence and the oil gradually incorporated by trituration, water being added from time to time if the emulsion thickens too much.

Emulsions prepared with yolk of egg are not so liable to separate upon the addition of alcoholic preparations, acid salts, diluted acids, glycerin, syrups or large quantities of soluble salts as are those prepared with acacia. Preservatives are necessary for this type of emulsion.

Yolk of egg may be preserved by mixing it with an equal volume of glycerin, and by this means it can be kept in a suitable condition ready for use.

When preparing an emulsion in an homogenising or emulsion machine, it may happen that the resulting emulsion is too viscous, although when made by hand in a mortar the viscosity is a suitable one. The difference is due to the much smaller globules of oil in the machine-made emulsion, and it is advisable in this case to reduce the amount of emulgent specified in the formula.

**ANTAGONISMS OF EMULSIFYING AGENTS.** Antagonisms sometimes occur between emulsifying agents which individually produce the same type of emulsion. Emulsifying agents may be divided into 3 groups: (1) emulsifiers with low internal and superficial viscosity (sodium oleate); (2) those with low internal and high superficial viscosity (saponin); (3) those with high internal and superficial viscosity (acacia). Members of group (1) antagonise the other groups, but groups (2) and (3) are compatible.—N. Chatterjee, per *J. Amer. pharm. Ass.*, 1937, 197.

**Methyl cellulose** is used for the preparation of oil-in-water emulsions. A 10% mucilage is prepared by heating the emulsifier with water and allowing to cool, or by wetting it with equivalent amount of glycerin, alcohol 90%, or oil, and then adding the water. The oil is then stirred into the mucilage. Emulsions prepared with methyl cellulose preparations are compatible with both acids and alkalis. Their mucilages are tasteless, neutral in reaction, do not ferment or grow moulds, and dry on the skin without unpleasant stickiness.

**P.M.B. 333** (*Pharmaceutical Specialities (May & Baker) Ltd., London*)  
A cellulose derivative colloiddally soluble in cold water, the solution becoming more viscous and less clear as the concentration of P.M.B. 333 increases. The solution has adhesive properties and can replace mucilages, agar-agar, tragacanth, acacia, etc. It is uniform, very stable, and has the power of emulsifying substances such as oils, fats, waxes, natural and artificial resins, etc.

For details of hand machines for preparing emulsions, see *Pharm. J.*, ii/1934, 307, 337.

## EPHEDRA

(with EPHEDRINE)

*B.P.C., Fr. Cx.*

*Syn. MA-HUANG.*

[P1] "*Alkaloids, the following; their salts, simple or complex:—Ephedra, alkaloids of.*"

[S3] "*Alkaloids—Ephedra, alkaloids of—in substances containing less than 1% of the alkaloids of ephedra.*"

[S6] "*Alkaloids—Ephedra, alkaloids of—specify proportion as the proportion of any one alkaloid of ephedra that the preparation would be calculated to contain on the assumption that all the alkaloids of ephedra in the preparation were that alkaloid.*"

The dried young branches of *E. sinica*, *E. equisetina*, *E. Gerardiana*, and other species of *Ephedra* (Ephedraceæ) from India, China and Spain. It contains 1 to 2% of alkaloids of which up to about 70% may be *l*-ephedrine, other alkaloids present being its stereoisomeride, *d-ψ*-ephedrine (pseudo-ephedrine), and small amounts of *l*-*N*-methylephedrine, *d*-*N*-methyl-*ψ*-ephedrine and nor-*d-ψ*-ephedrine. The *B.P.C.* requires not less than 1.25% of alkaloids.

Ephedra varieties and alkaloid content.—*Pharm. J.*, ii/1927, 118.

[P1] **Extractum Ephedræ Liquidum** (*B.P.C.*).

*Dose.*— $\frac{1}{2}$  to 1 drachm (1 to 4 ml.). 1 in 1.

When dispensed in mixtures mucilage must be added.

**Phedros** (*Sharp & Dohme, London*). Each fl. oz. contains chloroform 2 m., liquid extract of ephedra 40 m., syrup of squill 180 m., syrup of ipecacuanha 40 m., ammonium chlorid 8 gr., and syrup of tolu. *Dose.*—2 teaspoonfuls every 2 or 3 hours.

[P1] **Ephedrina** (B.P.C., U.S.P. XI, Fr. Cx.).

Syn.  $\alpha$ -HYDROXY- $\beta$ -METHYLAMINOPROPYLBENZENE,  $\alpha$ -PHENYL- $\beta$ -METHYL AMINOPROPANOL, *l*-EPHEDRINE.

$C_9H_9 \cdot CH(OH) \cdot CH(NH \cdot CH_3) \cdot CH_3 = 165.1$ .

**Dose.**— $\frac{1}{4}$  to  $1\frac{1}{2}$  grains (0.016 to 0.1 g.).

An alkaloid obtained from various species of *Ephedra*, and also prepared synthetically. The synthetic or artificial substance is laevorotatory and is stated to be identical in action with natural ephedrine (see E. C. Dodds and R. L. Noble, *Pharm. J.*, i/1938, 641). It occurs in white crystals which readily absorb moisture and carbon dioxide. As usually supplied it contains about 5% of water of crystallisation corresponding to the hemihydrate which has a m.p. of about 40°; the anhydrous crystals melt at about 38°. The hydrated crystals can be dried by storage over calcium chloride. (N.N.R. also gives EPHEDRINE ANHYDROUS and EPHEDRINE HEMIHYDRATE, both for use in a 1% oily solution for local application to mucous membranes.)

**Volatility.** Both ephedrine and pseudoephedrine are appreciably volatile at 30° and 60°C, and readily volatile at 100°C.—R. Monnet and P. Durand, per *Quart. J. Pharm.*, 1938, 764.

**Soluble** 1 in 20 of water, 1 in 20 of glycerin, 1 in 100 of liquid paraffin (the solution being turbid unless made with anhydrous ephedrine), and in light petroleum, ether, alcohol and fixed and volatile oils. The solution in chloroform leaves a residue of ephedrine hydrochloride on evaporation.

**Dispensing Note.** Ephedrine preparations should be kept in stoppered amber bottles. Aqueous solutions undergo decomposition on exposure to light and air with formation of benzal-ephedrine. Oily solutions give very unpleasant-smelling compounds, probably amines, and eventually ephedrine carbonate and ammonia.

**Compatibility.** Both the sulphate and hydrochloride appear to be compatible in the cold with chemicals likely to be prescribed with them, e.g., the bromides, iodides, carbonates, bicarbonates, and sodium salicylate. Reasonable precautions are needed as ephedrine is a delicate alkaloid.

**Toxic effects** have sometimes been observed, consisting of giddiness, headache, thirst, nausea, palpitation, insomnia, tremor, anxiety complex, and bladder irritation. Large and repeated doses should be avoided. Some patients need carefully regulated doses. Very large doses cause diaphoresis. For an adult a strong saline purge is suggested and a vasodilator if blood pressure is high, which is *not necessarily the case*.

Chronic poisoning following  $\frac{1}{4}$  grain thrice daily for four months.—W. H. Higgins, *J. Amer. med. Ass.*, i/1929, 313.

10 mg. of ephedrine subcutaneously may cause gangrene and necrosis at the site of injection, but smaller doses do not. Adrenaline is said to be two and a half times as efficient as ephedrine.—J. E. Nadler, *Pharm. J.*, ii/1927, 73.

**Uses.** Ephedrine has a similar physiological action to adrenaline, but its action is less potent and more prolonged and owing to its greater stability it has the advantage over adrenaline of being

effective when taken by the mouth. In therapeutic doses it has a stimulant action on the heart, but large doses are depressant. Given by injection it causes a lasting rise of blood pressure, and it is employed for this purpose to combat the fall in blood pressure consequent on spinal anaesthesia. Given orally or by injection it dilates the bronchial muscles and is of great value in asthma, though it is more effective in preventing an attack than in relieving one already present. It is of value in whooping-cough by relieving the bronchial spasm, though its effect is enhanced by the concurrent use of belladonna.

It has a similar vasoconstrictive action on mucous membranes to adrenaline, but is without the irritant action of the latter. Ephedrine sprays are much employed in hay fever, coryza and laryngitis, but their continued use is liable to lead to an aggravation of the dilatation; in particular, the use of oily sprays in children is to be deprecated, owing to the danger of lung complications.

It is also given internally in nocturnal incontinence, in myasthenia gravis and in narcolepsy, and has been suggested for use intravenously in obstetric shock and collapse and orally for the relief of nerve pains in leprosy. It is sometimes used as drops (1 or 2%) or ointment for its mydriatic effect.

It was found in barbiturised dogs that ephedrine administered either orally or intravenously has no effect on the intestinal absorption of isotonic sodium chloride solution or of isotonic glucose solution. Ephedrine given orally has no effect on absorption of water from the intestine, but when the drug is given intravenously the amount of water absorption is somewhat decreased. Since ephedrine has so little effect on the absorption of such divergent substances as water, sodium chloride and glucose, it seems safe to assume that the absorption of food substances in general from the intestine is probably not materially affected by the drug. This is of importance, as ephedrine is often given over long periods of time in certain chronic ailments.—E. J. van Lier, D. Northup and C. K. Sleeth, *J. Pharmacol.*, 1937, 434.

**ASTHMA.** Though it has the advantage over adrenaline of effectiveness *per os* and giving longer immunity from attacks, it may cause tremor, palpitation, insomnia and sometimes inability to micturate.—Frank Coke, *Brit. med. J.*, i/1929, 954. The first dose seems to act marvellously, but subsequent doses seem to do nothing.—J. Freeman, *ibid.*

A useful prophylactic agent. Psychological effect of being able to prevent acute attack. Peptone injections prior to ephedrine of value.—A. Dingwall Fordyce, *Brit. med. J.*, i/1931, 166.

The following injection hypodermically has been found useful in severe attacks.—Ephedrine hydrochloride  $\frac{1}{2}$  gr., Liq. Adrenalin. 1 in 1000 5 m., pituitary extract 0.5 ml., distilled water to 1 ml. It should be put up in air-free ampoules, as otherwise it becomes discoloured.—M. W. Geffen, *Lancet*, ii/1932, 56.

Definitely better results when combined with thyroid medication.  $\frac{1}{2}$  gr. dose of ephedrine hydrochloride twice daily gave little relief, but  $\frac{1}{2}$  gr. dose at night with 1 gr. of thyroid B.P. in the morning averted attacks for some months.—H. S. Russell, *Brit. med. J.*, i/1934, 1097.

**COLIC.** Ephedrine hydrochloride is preferable to morphia in both renal and biliary colic. In renal colic the results of  $\frac{1}{2}$  to 1 gr. dose of ephedrine by mouth are spectacular—relief is almost instantaneous. In gall-stone colic there is some relief, but not to the same extent as is the case with renal colic. If ephedrine is not available,  $\frac{1}{2}$  gr. atropine sulphate acts very well, *i.e.*, it acts on the unstriated muscle fibre and relaxes the muscle.—A. J. Ambrose, *Med. Pr.*, ii/1936, 46.

**ENURESIS IN CHILDREN.** Ephedrine  $\frac{1}{2}$  grain at bedtime for child from 10 to 12 almost specific. Bladder emptied before and 2 hours after going to sleep.—L. E. Parkhurst, *Brit. med. J.*, ii/1930, 1103.



The most useful drug at present available for treatment of enuresis in children. Give an initial dose of ephedrine hydrochloride at bedtime and increase by  $\frac{1}{2}$  gr. every 4 to 7 days till enuresis is controlled; as much as 4 gr. at a dose given without unpleasant effects. Wakefulness and restlessness respond well to phenobarbitone  $\frac{1}{2}$  gr. given with the ephedrine.—R. W. Brookfield, *Brit. med. J.*, ii/1935, 1119.

Ephedrine was given in 38 consecutive cases, over periods up to several months: the enuresis ceased in 10 cases and there was improvement in 14 others. The ephedrine sometimes caused restlessness and other side-effects, but these were seldom seen in older children of phlegmatic type, some of whom seemed to have an unusual tolerance to the drug. Toxic effects cease promptly when the drug is remitted. Those cases in which enuresis persists through school life, only to cease in the late teens or early twenties, are precisely the ones in which ephedrine appears to be of most value. After excluding urinary infection, half a grain of ephedrine alkaloid in tablet form is prescribed to be given at bedtime. The dose is increased by  $\frac{1}{2}$  gr. every 3 to 4 nights until in some cases as much as 5 grains is being taken. The insomnia due to ephedrine may be relieved to some extent by giving  $\frac{1}{2}$  to 1 gr. of phenobarbitone simultaneously.—R. W. Brookfield, *Lancet*, ii/1937, 623.

LEPROSY. *Per os* relieves nerve pains. More lasting and efficient than adrenaline injections.—E. Muir, *Indian med. Gaz.*, Apr., 1928, 198. See also R. G. Cochrane, *Lancet*, ii/1929, 551, and R. Green, *Trans. R. Soc. trop. Med.*, Jan., 1929, 376.

LOW BLOOD PRESSURE.  $\frac{1}{2}$  to  $\frac{1}{4}$  gr. produces very satisfactory rise in pressure and no toxic symptoms.  $\frac{1}{2}$  gr. caused giddiness.—H. W. Hales, *Lancet*, ii/1928, 360.

Chronic vascular hypotension. Nine cases treated. Rise in systolic pressure, remaining up for 4 hours.—*Lancet*, ii/1928, 144.

Doses of 0.05 to 0.125 g. *per os* or subcutaneously raise systolic and diastolic blood pressure, and increase pulse rate for several hours.—T. G. Miller, *per J. Amer. med. Ass.*, ii/1925, 1159.

Low blood pressure following influenza, pneumonia, etc. The power of ephedrine to raise blood pressure appears to be decreased in arteriosclerosis, debility and hypertension.—*J. Amer. med. Ass.*, 1931, 96, 480.

Warning against use in patients with cardiac injury.—*Prescriber*, 1929, 70.

MYASTHENIA GRAVIS. Personal experience of a medical victim after influenzal pneumonia. Progress with ephedrine after none with adrenaline and thyroid.—H. Edgeworth, *J. Amer. med. Ass.*, i/1930, 1136.

Ephedrine in doses of  $\frac{1}{2}$  gr. twice daily of distinct value, the disease may, however, progress during its use.—D. McAlpine, *Lancet*, i/1934, 180.

NARCOLEPSY. Symptoms successfully treated in eight cases by ephedrine hydrochloride or sulphate  $\frac{1}{2}$  gr. 2 or 3 times daily.—Henry Cohen, *Lancet*, ii/1932, 335. See also A. Haddow, *ibid.*, 420.

OBSTETRIC SHOCK AND COLLAPSE. 1 gr. in 8 ml. of normal saline intravenously. Also in gynaecological cases to lessen shock of operation.—J. H. Hannon, *Brit. med. J.*, i/1929, 954.

SHOCK FROM TRAUMA OR HÆMORRHAGE. Intravenous injection of 15 mg. of value.—C. A. Johnson, *J. Amer. med. Ass.*, i/1930, 1388.

SPINAL ANÆSTHESIA. Of value in restoring arterial tension. Give 0.1 g. subcutaneously before systolic pressure drops below 100.—*J. Amer. med. Ass.*, 1927, 1136.

For dependable results (to raise blood pressure in spinal anæsthesia) ephedrine must always be given intravenously, because its action is uncertain when given intramuscularly or subcutaneously. The duration of the raised level is uncertain, 10 to 20 minutes being probably the maximum period; therefore, repeated injections are necessary.—H. Dodd, *Lancet*, i/1940, 359.

STOKES-ADAMS' DISEASE. 30 mg. of ephedrine sulphate by mouth gave instant relief from attacks and in one week the individual dose was cut down to 20 mg. Medication ceased after a fortnight and there were no attacks for a year, when they were again relieved by ephedrine.—C. S. Higley and R. M. Stechen, *per Brit. med. J. Epi.*, i/1934, 27.

In six cases of complete heart-block ephedrine orally increased the rate of ventricular beating in four, and in two other cases complicated by Stokes-Adams' seizures, ephedrine taken for 2 $\frac{1}{2}$  and 1 $\frac{1}{2}$  years respectively was entirely

successful in prevention of syncopal attacks, but seizures returned with its discontinuance. The dose recommended is the minimum quantity consistent with an acceleration. A dose of  $\frac{1}{2}$  gr. at 8-hour intervals may be sufficient.—A. R. Gilchrist, *Brit. med. J.*, i/1934, 613.

**WHOOPING COUGH.** Dose of  $\frac{1}{2}$  grain *per os* in watery solution to children of one year and  $\frac{1}{4}$  grain for those younger, night and morning, of value. Most useful during second stage. No serious toxic symptoms.—*Brit. med. J. Epit.*, i/1928, 28.

**Narist. Ephedrin. (N.I.F.).** Ephedrine  $2\frac{1}{2}$  gr., menthol  $1\frac{1}{2}$  gr., oleic acid 5 m., liquid paraffin to 1 oz.

[P1] **Nebula Adrenalinae et Ephedrinae Oleosa (B.P.C.).**

Adrenaline 1 in 10,000 and ephedrine 1 in 50, with menthol and eucalyptol in an oily basis.

A warning concerning the misuse of vasoconstrictor drugs (adrenaline and ephedrine) as sprays, oils or drops for nasal troubles. Continuous and indiscriminate use may be fraught with disastrous results. On repeated use the duration of the constriction becomes gradually reduced, and in the end a condition of aggravated dilatation is produced.—A. Francis, *Brit. med. J.*, i/1936, 609.

Solutions of drugs in oils should never be used as intranasal medication, in infants and children, and should be used with care in adults. Antiseptic solutions are of doubtful value in decreasing the pathogenic flora of the nose, and there is danger of producing lung lesions. Ephedrine is a chemically stable vasoconstrictor which in normal saline solution does not produce the unpleasant sensation of burning and stinging. These qualifications render it specially suitable for use in children.—C. G. Flake, *New Engl. J. Med.*, 1939, 866.

An attempt to produce antiseptic or astringent effects in the nose with any of the solutions now in use is fraught with danger, and weak solutions of ephedrine ( $\frac{1}{2}$  per cent. in normal saline) are the only ones which should justifiably be used to produce vasoconstriction, since these alone neither damage ciliary action nor interfere with the flow of mucus.—*Brit. med. J.*, i/1939, 343.

[P1] **Neb. Ephedrin. Co. (N.I.F.).** Ephedrine  $4\frac{1}{2}$  gr., menthol  $8\frac{1}{2}$  gr., camphor  $8\frac{1}{2}$  gr., oil of thyme 9 $\frac{1}{2}$  m., oleic acid 10 m., light liquid paraffin to 1 oz.

[P1] **Nebula Ephedrinae Composita (B.P.C.).** Ephedrine 1% *w/v* with menthol, camphor and oil of thyme in light liquid paraffin.

[P1] **Unguentum Ephedrinae (B.P.C.).** 1% in white soft paraffin.

[P1] **Ephetonin (Merck, Darmstadt; Savory & Moore, London)** is the inactive form of ephedrine synthetically prepared. 4 mg. of the synthetic are stated to be equivalent to 2 mg. of the natural alkaloid.

[P1] **Ephedrinae Hydrochloridum (B.P., U.S.P. XI, Fr. Cx., P. Helv. V, P. Dan.).**

$C_6H_5 \cdot CH(OH) \cdot CH(NH \cdot CH_3) \cdot CH_3 \cdot HCl = 201.6$ .

**Dose.**— $\frac{1}{2}$  to  $1\frac{1}{2}$  grains (0.016 to 0.1 g.). (*Caution:* 1 grain has been known to produce slight toxic phenomena. Many people react well to  $\frac{1}{10}$  grain.) *U.S.P. XI* average dose  $\frac{3}{4}$  grain. *P. Dan.* max. single dose  $1\frac{1}{2}$  grains; max. per day 6 grains. *P. Helv. V* gives  $\frac{3}{4}$  grain and 3 grains respectively. Colourless crystals. M.p.  $213^{\circ}$  to  $216^{\circ}$ .

**Soluble** 1 in 5 of water, 1 in about 5 of alcohol 90%, 1 in 60 of glycerin; insoluble in ether, chloroform, olive oil and in liquid paraffin.

**Ephedrine-Glucose-Gum Solution.** Advocated for intravenous infusion following severe hæmorrhage.—Ephedrine hydrochloride 1 gr., dextrose 440 gr., acacia 525 gr., water to 1 pint. The ephedrine is stated to help to raise the peripheral resistance, thus raising the blood pressure more rapidly. Insulin (10 units) may be given intramuscularly at the same time.—W. Hunter, *Brit. med. J.*, ii/1936, 537.

**Elixir Ephedrinæ Hydrochloridi (B.P.C.).**

*Dose.*— $\frac{1}{2}$  to 2 drachms (2 to 8 ml.).

A lemon-flavoured elixir containing  $\frac{1}{2}$  gr. of ephedrine hydrochloride per dr. Asthma is well treated by 1 to 2 drachms at bedtime; also gives relief in hay fever. For whooping-cough in children  $\frac{1}{2}$  to 1 drachm.

**[P1] Nebula Adrenalinæ et Ephedrinæ (B.P.C.).**

Adrenaline 1 in 8000 and ephedrine hydrochloride 1 in 45 in an aqueous medium.

**[P1] Tabellæ Ephedrinæ Hydrochloridi (B.P.C.) contain  $\frac{1}{2}$  gr. (0.03 g.).**

[P1] **Adrephine Inhalant** (*Parke, Davis, London*). Adrenaline 1 in 10,000, ephedrine hydrochloride 1%, benzocaine 1%, Chloretone 0.5% and glycerin q.s. As a spray in hay fever, rhinitis, etc. [P1] **Adrephine Ointment** contains adrenaline 1 in 5000 and ephedrine hydrochloride 2%. For application to inflamed mucous membrane.

**Argotone** (*Rona Laboratories, London*). "Natural laevorotatory Ephedrine hydrochlorate" 0.9%, Argryol (Barnes) 1, normal saline solution to 100. To be used as a spray at least two times daily or 4 to 6 drops to be instilled into each nostril 3 to 5 times a day.

[P1] **Cosme Brand Cough Syrup** (*Merck, Darmstadt; Savory & Moore, London*). Contains Ephetonin 0.2%, Dionin 0.04%, and syrup of thyme.

[P1] **Disco** (*Abbott Laboratories, London*). Tablets containing ephedrine hydrochloride  $\frac{1}{2}$  gr. and phenacetin  $1\frac{1}{2}$  gr. *Dose.*—2 tablets and then one tablet at intervals of 1 to 4 hours, as required. For relief of pain in dysmenorrhœa.

[P1] **Ephetonogen** (*Richter, London*). Ephedrine hydrochloride 0.02 g., adrenaline 0.0001 g. *Dose.*—1 ml. daily subcutaneously or intramuscularly.

[P1] **Ephetonogen Forte**. Ephedrine hydrochloride 0.03 g., adrenaline 0.00015 g., atropine 0.00002 g., in 1 ml. *Dose.*—1 ml. subcutaneously or intramuscularly.

[P1] **Ephregal** (*Evans, Sons, Lescher & Webb, Liverpool*). A combination of ephedrine and adrenaline as a nasal jelly for use in hay fever, rhinitis, and acute colds.

[P1] **Ephrelux** (*Evans, Sons, Lescher & Webb, Liverpool*). Elixir containing per dr. ephedrine hydrochloride  $\frac{1}{2}$  gr., codeine phosphate  $\frac{1}{12}$  gr., with squill and wild cherry. *Dose.*—2 to 4 drachms.

[P1] **Ephresol** (*Evans, Sons, Lescher & Webb, Liverpool*). Nasal spray containing ephedrine hydrochloride 2% and adrenaline 0.01%.

**Ephretuss** (*Evans, Sons, Lescher & Webb, Liverpool*). Syrup of ephedrine containing  $\frac{1}{2}$  gr. of ephedrine per dr. *Dose.*—Under 1 year, up to 1 drachm; over 1 year, up to 2 drachms; 2 or 3 times daily.

[P1] **Gluco-Fedrin** (*Parke, Davis, London*). A nasal spray containing ephedrine 1%, chloretone 0.5%, and menthol 0.1% in a dextrose base. For the treatment of rhinitis, etc.

[P1] **Isedrin Plain** (*Lilly, London*). Aromatic aqueous solution of ephedrine 1% w/v, with gluconic acid and chlorbutol 0.5%, rendered isotonic with dextrose, for use as a nasal spray in catarrh, etc. Available also with Merthiolate (Isedrin Compound) instead of chlorbutol.

[P2] **Metaphedrin Inhalant No. 99** (*Abbott Laboratories, London*). Contains ephedrine 0.95% and Metaphen (q.v.) 1 in 2500. Colds, asthma, hay fever, etc.

[P1-81-84] **Ephedrine and Nembital** (*Abbott Laboratories, London*). Capsules containing Nembital  $\frac{1}{2}$  gr. and ephedrine hydrochloride  $\frac{1}{2}$  gr. Asthma, hay fever, and other allergic conditions. The addition of Nembital has antispasmodic and sedative effect.

**Zephrol** (*Pharmaceutical Specialities (May & Baker) Ltd., London*). Nasal jelly containing ephedrine hydrochloride, chlorbutol, sodium chloride and essential oils. Zephrol spray solution and cough syrup, both containing ephedrine, are also supplied.

[P1] **Ephedrinæ Sulphas** (B.P.C.).  $(C_{10}H_{15}ON)_2 \cdot H_2SO_4 = 428.3$ .

*Dose.*— $\frac{1}{4}$  to  $1\frac{1}{2}$  grains (0.016 to 0.1 g.). U.S.P. XI average dose  $\frac{1}{2}$  grain.

White, colourless, odourless crystals, **soluble** 1 in 2 of water, 1 in 60 of alcohol 90%, 1 in 60 of glycerin; insoluble in oils.

[P1] **Adrephine** (Parke, Davis, London). Adrenaline 0.01%, ephedrine sulphate 2% and Chloretone 0.5% in solution. Used as spray in hay fever, rhinitis, etc.

[P1] **Epinalin** (Burroughs Wellcome, London). Each ml. contains adrenaline 0.0001 g. (= 1 in 10,000) and ephedrine sulphate 0.02 g. (= 1 in 50). Nasal spray in asthma and hay fever. Also supplied in ampoules for hypodermic injection.

[P1] **Pseudo-Ephedrine**. *Syn.* *d-ψ*-EPHEDRINE.

*Dose.*—Children:  $\frac{1}{4}$  grain (0.015 g.) for children under 7,  $\frac{1}{2}$  grain (0.03 g.) for children over 7. Adults: 1 grain (0.06 g.) repeated at hourly intervals until 3 grains has been given.

Less toxic than ephedrine and much less effect on blood pressure. Is more effective in lessening frequency of attacks in asthma of children, but not so effective in relieving an attack in adults. Useful for prevention of dyspnoea in bronchitis and bronchial asthma. Especially indicated in those cases intolerant of ephedrine.

PRESSOR ACTION IN MAN was determined in 28 patients by subcutaneous injection. 1 gr. of pseudo-ephedrine caused a slight rise of blood pressure followed by a fall, while 2 gr. produced a pronounced rise approximating to that obtained with 1 gr. of ephedrine.—S. B. Dimson, *Quart. J. Pharm.*, i/1934, 23. (Report to the Therapeutic Trials Committee.)

Pseudo-ephedrine is of less value than ephedrine for controlling a fall in blood pressure during spinal anaesthesia.—J. E. Monroe, *ibid.*, 32.

PSEUDO-EPHEDRINE IN ASTHMA. A report to the Therapeutic Trials Committee. *Per os* it is more efficacious than ephedrine in lessening attacks of asthma in childhood, but less efficacious in relieving actual asthmatic paroxysm in adults. Less toxic than ephedrine, but in large doses may produce the same unpleasant side-actions. Worthy of further trial in children and in adults unable to tolerate ephedrine. Neither ephedrine nor pseudo-ephedrine as effective as adrenaline injections in treatment of an asthmatic attack.—G. W. Bray and L. J. Wirts, *Lancet*, i/1934, 790.

Tests of ephedrine and pseudo-ephedrine at the Hospital for Sick Children, Gt. Ormond Street, find both drugs wanting as a sure preventive of asthmatic attacks, the best medicinal treatment for children being dilute hydrochloric acid before meals, with an anti-spasmodic at bedtime.—Asthma Research Council Report, 1933, *Brit. med. J.*, ii/1933, 1135.

Useful for the minor manifestations of asthma but cannot replace ephedrine in the severe attacks.—J. B. Christopherson and M. Broadbent, *Brit. med. J.*, i/1934, 978.

**Propadrinæ Hydrochloridum**. *Prop. Name.* PROPADRIN HYDROCHLORIDE (Sharp & Dohme, London) (Capsules contain  $\frac{1}{2}$  gr.).  $C_6H_5 \cdot CHOH \cdot CHNH_2 \cdot CH_3 \cdot HCl = 187.7$ .

*Dose.*— $\frac{1}{4}$  to  $\frac{1}{2}$  grain (0.024 to 0.048 g.).

Propadrine hydrochloride is the hydrochloride of *dl*-phenyl-1-amino-2-propanol-1, a base resembling ephedrine. It occurs as a white, crystalline powder, melting at  $190^\circ$  to  $194^\circ$ .

**Soluble** freely in water and alcohol; insoluble in ether, chloroform and benzene.

**Uses.** Has an action similar to that of ephedrine but somewhat

more prolonged, and is less apt to give rise to an anxiety complex. It is employed internally in the treatment of allergic manifestations. Externally, it has a vasoconstrictive action on the mucous membranes and is used by local application in rhinitis, etc., in the form of a 1% solution or as a compound nasal jelly containing 0.66% of the hydrochloride.

**Amphetamina.** *Syn. and Prop. Names.* ISOMYN,  $\beta$ -AMINO-PROPYLBENZENE,  $\beta$ -PHENYLISOPROPYLAMINE, BENZYL METHYL CARBINAMINE,  $\alpha$ -METHYLPHENETHYLAMINE,  $\alpha$ -PHENYL- $\beta$ -AMINOPROPANE, RACEMIC DESOXY-NOR-EPHEDRINE, ALLODENE (*Bush, London*), BENZEDRINE (*Smith, Kline & French, Philadelphia; Menley & James, London*).

[P1] and [S1] "*Beta-aminopropylbenzene; its salts; its N-alkyl derivatives; their salts; beta-aminoisopropylbenzene; its salts; its N-alkyl derivatives; their salts.*"

[S3] "*Beta-aminopropyl benzene; its salts; its N-alkyl derivatives; their salts; beta-aminoisopropylbenzene; its salts; its N-alkyl derivatives; their salts, in appliances for inhalation in which the poison is absorbed in inert solid material.*"

[S7] "*Medicines made up ready for the internal treatment of human ailments containing beta-aminopropylbenzene; its salts; its N-alkyl derivatives; their salts; beta-aminoisopropylbenzene; its N-alkyl derivatives; their salts, must be labelled with the words "Caution. It is dangerous to take this preparation except under medical supervision" instead of the word "poison."*"

A colourless, mobile liquid with a slight odour and an acrid taste, obtained by the reduction of the oxime of phenylacetone. Amphetamine consists of a mixture of racemic desoxy-nor-ephedrine bases of the formula  $C_6H_5CH_2CH \cdot NH_2 \cdot CH_3$ . It readily volatilises at the ordinary temperature and boils at about  $202^\circ$ . On exposure to air it absorbs carbon dioxide forming a carbonate which is also readily volatile.

Slightly **soluble** in water; soluble in ether, alcohol, acids, amyl alcohol, ethyl acetate and chloroform.

**Uses.** It resembles ephedrine and adrenaline in properties, and is used as a volatile vasoconstrictor for use by inhalation in hay fever and for the relief of acute coryza and all catarrhal affections of the respiratory system. Inhalations should be repeated at not less than hourly intervals, since overdosing may give rise to restlessness and insomnia. Its use is contraindicated in cardiovascular disease, and in patients suffering from sinusitis it is stated to increase the severity of the symptoms.

An exhaustive list of the toxic signs and symptoms due to the inhalation of Benzedrine.—S. P. Waud, *J. Amer. med. Ass.*, i/1938, 206.

**Benzedrine Inhaler** (*Smith, Kline & French, Philadelphia; Menley & James, London*). An inhaler containing  $\beta$ -phenylisopropylamine 0.325 g., oil of lavender and menthol.

**Karsodrine Inhaler** (*Griffiths Hughes, Manchester*). An inhaler containing  $\beta$ -phenylisopropylamine 0.33 g., cineol, oil of citronella, methyl salicylate, oil of eucalyptol, menthol and eucalyptol.

[P1-31] **Amphetaminæ Sulphas.** *Prop. Name.* BENZEDRINE SULPHATE (*Smith, Kline & French, Philadelphia; Menley & James, London*).

*Dose.*— $\frac{1}{24}$  to  $\frac{1}{2}$  grain (0.0025 to 0.01 g.).

A white odourless powder with a slightly bitter taste that is followed by numbness. It is prepared by neutralising benzedrine in alcoholic solution with sulphuric acid.

Readily **soluble** in water; slightly soluble in alcohol (90%); insoluble in ether.

**Toxic Effects.** It is usually well tolerated in therapeutic dosage, but minor reactions such as dryness of the mouth, insomnia, loss of appetite, tremor and palpitations are not uncommon. Overdosage may lead to collapse and syncope, and continuous administration may lead to addiction, and has been known to give rise to aplastic anæmia.

Untoward cardiovascular effects were observed following the administrations of 10 to 30 mg. of Benzedrine sulphate. Symptoms included pallor, flushing, palpitation and variations in pulse-rate and blood-pressure. In six cases the effects recorded included collapse, multiple extrasystoles, heart-block and pain in the chest radiating to the left arm.—E. W. Anderson and W. C. N. Scott, *Lancet*, ii/1936, 1461.

Symptoms of acute poisoning were brought on in one case as a result of the ingestion of 30 mg. within six hours.—H. Ulrich, *New Engl. J. Med.*, ii/1937, 696.

Benzedrine sulphate gives the best results when used in doses of 10 to 30 mg. Larger amounts often produce so much palpitation, tremor and rise in blood pressure that the concomitant psychological effects are apt to be destroyed. The drug should be given before midday if sleeplessness is to be avoided; the effect tends to remain at a maximum for about 5 hours and takes an hour or more to develop fully. The possibility of addiction needs to be guarded against, though the preponderance of disquieting somatic symptoms over the feeling of euphoria, when large doses are taken, and the sleeplessness induced will probably make addiction rare.—E. Guttman and W. Sargent, *Brit. med. J.*, i/1937, 1013.

A case of acute aplastic anæmia following the self-administration of Benzedrine sulphate by a young man of 26, previously in good health. The total amount taken was 190 mg. in nineteen days. Severe cardiovascular collapse occurred the day after the last dose was taken. Gradual recovery ensued with restoration to normal health.—I. J. Davies, *Brit. med. J.*, ii/1937, 615.

Collapse with death following continued use of Benzedrine sulphate by a student.—L. C. Smith, *J. Amer. med. Ass.*, ii/1939, 1022.

The continued use of amphetamine may result in addiction. A case reported.—S. Friedenber, *J. Amer. med. Ass.*, i/1940, 956.

**Contraindications.** Its use is contraindicated in elderly patients, in cardiovascular disease, especially in the presence of hypertension, and in patients with prominent anxiety symptoms.

**Uses.** Amphetamine sulphate has a marked stimulant effect on the central nervous system, causing a lessening of fatigue, an increase of mental activity, and a general feeling of well-being; in the higher doses it causes an appreciable rise in blood pressure and relaxes the smooth muscle of the gastro-intestinal tract. The pressor effect is enhanced by atropine, stramonium and scopolamine. It has been employed with success in the treatment of narcolepsy, in post-encephalitic parkinsonism, in sea-sickness, and in mild depressive neuroses. It is not recommended in the treatment of sleepiness and fatigue in normal individuals, and should not be used as a "pick-me-up," except under strict medical

supervision. In maximum doses it is of value for facilitating the roentgenographic study of the intestinal tract, but its general use in spastic conditions of the intestine is not recommended.

It is best to commence treatment with a dose of from 2.5 to 10 mg., and it is inadvisable to exceed 20 mg. for a single dose. In certain conditions it may be necessary to repeat the use of the drug two or three times daily. In order to avoid insomnia the drug is preferably administered during the morning.

**BARBITURATE POISONING.** Benzedrine sulphate is effective in preventing or counteracting the narcosis produced by the intravenous administration of sodium amytal. This action and the fact that Benzedrine sulphate causes a rapid and prolonged rise in blood pressure may be found useful in certain medical or surgical cases in which it seems desirable to overcome severe side reactions of the narcosis produced by the barbiturates, particularly respiratory embarrassment and pronounced decrease in blood pressure.—A. Myerson *et al.*, *New Engl. J. Med.*, ii/1939, 1015.

**HYPOTENSION.** An investigation of blood pressure in mental disorders. Benzedrine sulphate given orally causes a rise in blood pressure, commencing in 45 to 120 minutes, reaching a maximum in a further 60 minutes and returning to normal in 24 hours. All patients showed increased talkativeness and frequently there was a tendency in the direction of euphoria.—S. A. Peoples and E. Guttmann, *Lancet*, i/1936, 1107.

**MORPHINE WITHDRAWAL TREATMENT.** The administration of Benzedrine sulphate, 10 mg. daily, is an invaluable aid in combating the physical and mental inertia which is a common factor during convalescence from drug addiction.—H. C. Duckworth, *Brit. med. J.*, ii/1940, 628.

**NARCOLEPSY.** Complete relief of attacks of sleep and almost complete relief of cataplexy obtained in nine cases from use of Benzedrine 10 to 40 mg. 3 times a day. Start with 10 mg. doses to avoid untoward symptoms. Approximately three times as effective as ephedrine in preventing attacks of sleep.—M. Prinzmetal and W. Bloomberg, *J. Amer. med. Ass.*, ii/1935, 205.

Oral medication with Benzedrine sulphate appears to be the only satisfactory method of treatment. Several cases of long-continued use are reported; no deleterious effects were noted, and there was no evidence of habit formation.—H. Ulrich, *New Engl. J. Med.*, ii/1937, 696.

**POST-ENCEPHALITIC PARKINSONISM.** Combined treatment with Benzedrine sulphate, 10 mg. daily, and atropine sulphate, 10 to 15 drops of 0.5% solution three times daily, gave better results in the symptomatic treatment of 12 cases than the use of either medicament alone.—J. Finkelman and L. B. Shapiro, *J. Amer. med. Ass.*, ii/1937, 344.

Sixty-six out of 74 patients obtained definite subjective benefit from the use of Benzedrine (either alone or combined with the belladonna group of drugs) and 53 obtained objective benefit. Two doses of Benzedrine sulphate were given daily, the first at 8 a.m. and the second at noon, the dose varying from 40 to 60 mg. a day, the age and systolic pressure of the patient being used as determining factors in prescribing the initial dose. While it may not produce the striking relief of symptoms seen with the atropine group, it has the advantage that a constant dose seems to be adequate and that it is free from distressing side effects.—F. L. Davis and W. B. Stewart, *J. Amer. med. Ass.*, i/1938, 1890.

Benzedrine enhances the effect of stramonium, atropine and scopolamine, and is best used in conjunction with these drugs in the treatment of post-encephalitic parkinsonism. Encouraging results in 20 cases.—R. A. Matthews, *Amer. J. med. Sci.*, 1938, 195, 448.

**PSYCHIATRY.** The immediate effects of Benzedrine sulphate administered orally in doses of 10 to 20 mg. before breakfast and frequently repeated at noon, have been studied in 100 cases in which there were disorders of mood (chiefly depression), chronic nervous exhaustion and psychoneurosis. In about 80% of the cases of chronic exhaustion or depression, the immediate results were favourable and in some instances spectacular. When given to psychoneurotic patients, particularly those who are anxious, highly nervous and apparently stimulated, it has a less favourable immediate effect.—D. L. Wilbur, A. R. MacLean and E. V. Allen, *Proc. Mayo Clin.*, 1937, 97.

An account of a study of the effects of Benzedrine on a group of 33 patients over a period of fourteen months who were suffering from the minor forms of mental disorder. The dosage varied from 5 to 45 mg. daily *per os*. In 16 the drug had to be discontinued owing to untoward effects, and in two more because no benefit was produced. In 11 the drug appeared to be helpful, and in 5 no effect, mental or physical, was produced. Apart from transient relief in some cases, the drug is of doubtful value as an aid to psychotherapy. It would appear unwise to give Benzedrine to any subject with prominent anxiety symptoms. The initial dose should not exceed 10 mg., and the optimum dose determined carefully (divided dosage is recommended). It should be used cautiously in certain depressives, because of the possibility of intensifying the depression, with consequent suicidal risk.—E. W. Anderson, *Brit. med. J.*, ii/1938, 60.

**SEA-SICKNESS.** In 100 cases of sea-sickness satisfactory results were obtained from the use of Benzedrine sulphate in 39, doubtful results in 40, and failure in 21. It is not a rival to old-established methods, but is a useful ally. The effect is greater and more lasting when combined with other remedies. The effect is augmented by vagus-inhibiting drugs such as belladonna, and in the presence of concomitant sympathetic activity bromides or barbiturates prevent unpleasant restlessness and insomnia without interfering with the gastro-intestinal or circulatory effects of Benzedrine.—J. Hill, *Brit. med. J.*, ii/1937, 1109.

**SPASTIC COLON.** Benzedrine sulphate is not recommended in the treatment of spastic disorders of the gastrointestinal tract. Of 18 patients with a spastic irritable colon treated with Benzedrine sulphate, 3 improved, 1 showed improvement followed by relapse, 11 were unimproved, and 3 were worse.—D. H. Rosenberg *et al.*, *J. Amer. med. Ass.*, 1/1938, 1994.

[P1-81] **Methedrine** (*Burroughs Wellcome, London*).

$C_6H_5 \cdot CH_2 \cdot CH(CH_3) \cdot NH(CH_3)$ . = 149-23.

**Dose.**—2 to 4 mg. every four hours until the desired effect is obtained.

Methedrine is the dextro-rotatory form of the N-methyl derivative of amphetamine. It is issued in 2 mg. tablets for the treatment of narcolepsy and for controlling symptoms similar to those of narcolepsy in the treatment of post-encephalitic parkinsonism. It has been used as an analeptic in barbiturate poisoning and appears to be useful in increasing energy or capacity for work. It must, however, be used cautiously, particularly owing to its pressor effect and the hyper-excitability, gastro-intestinal disturbance and sleeplessness which follows its administration.

Its use is **contraindicated** in cardio-vascular disease, especially when hypertension is present.

**Par-Isalon** (*Coates & Cooper, London*). Tablets containing Isalon (1-phenyl-2[methyl(diethylaminoethyl)]-aminopropane-1-ol—*Gehe*), theobromine, caffeine and phenazone. For bronchial asthma, chronic bronchitis, angina pectoris, etc.

**Isalon** is an ephedrine substitute stated not to have the blood-pressure-raising effect of ephedrine, but to have a good action on the bronchial muscles. Of 60 cases treated (0.09 g. in tablets thrice daily during attacks and half this dose during quiescent periods) 22 were cured and 28 much relieved, with no observable effect on blood pressure or pulse rate and no toxic symptoms.—H. Handovsky and E. Kubeja, *Munch. med. Wschr.*, 1934, 326.

**Phedracin** (*Ciba, Horsham*). (Formerly known as CIBA 2020.) The hydrochloride of trimethoxybenzyl-dihydroimidazol; distantly related to adrenaline, ephedrine and mescaline. **Dose.**—Orally (tablets containing 0.2 g.), 0.1 to 0.4 g.; intramuscularly (1 ml. ampoules contain 0.1 g.), 0.1 to 0.2 g.; intravenously, 0.1 g. To combat the fall of blood pressure in spinal anaesthesia and for the treatment of post-operative shock; also in cases, e.g., asthma, where patients are refractory to or intolerant of ephedrine.

In laboratory animals it was found to produce prolonged elevation of the blood pressure. In man it appears to act predominantly on the smooth muscle of the blood vessels and skin, producing a rise in blood pressure, pallor, and goose-skin.



its action on the bronchial musculature renders it of some value in asthma, but it appears to be inferior to ephedrine, though it may be useful as an alternative when ephedrine is contraindicated or inactive. It has been found helpful in controlling the blood pressure during spinal anaesthesia, and in the treatment of operative shock.—F. A. Jones and C. Wilson, *Lancet*, i/1938, 195.

**Euphorbia (B.P.C.).** *Syn.* AUSTRALIAN SNAKE WEED, CAT'S HAIR, EUPHORBIA PILULIFERA. The dried entire plant, *E. hirta* (Euphorbiaceæ).

For asthma, bronchial affections, paroxysmal dyspnoea, laryngeal spasm, whooping cough, angina pectoris, coryza and hay fever.

**Euphorbia Extract (Aqueous).** *Dose.*— $\frac{1}{2}$  to 1½ grains. **Tincture.** *Dose.*—10 to 30 minims. 1 in 5 of alcohol 60%.

**Extractum Euphorbiæ Liquidum (B.P.C.).**

*Dose.*—2 to 5 minims (0.12 to 0.3 ml.). 1 in 1. The *N.F. VI* dose for a liquid extract of the same strength is 30 minims.

[P1] **Mist. Euphorb. Co. (N.I.F.).** Potassium iodide 7½ gr., sodium bromide 7½ gr., liquid extract of euphorbia 10 m., solution of glyceryl trinitrate 1 m., ethereal tincture of lobelia 7½ m., water to ½ oz.

**Euphorbia Peplus (Euphorbiaceæ).** *Syn.* PETTY SPURGE, DEVIL'S MILK. The entire plant. Indigenous to the British Isles.

In cases of dyspnoea, whether of pulmonary or pneumogastric origin. Modifies secretion in asthma and suppresses attacks. The fresh plant has an acrid juice which, when dried, imparts its virtues both to water and alcohol. **Decoction**—45 grains to the pint. *Dose.*—1 teacupful (diluted if preferred) 3 or 4 times daily, preferably between meals. **Extract.** *Dose.*—7½ to 30 grains. **Tincture** (1 in 5 with 45% alcohol). *Dose.*—30 to 60 minims during the day.

**Euphorbium (B.P.C., Fr. Cx.).** Dried latex obtained by incision from the stem of *Euphorbia resinifera* (Euphorbiaceæ).

It occurs in dull yellowish-brown tears, brittle, odourless, and with an acrid taste. The powder is sternutatory. It is used as a vesicant in veterinary practice.

**Costus.** *Syn.* KUNTH, KUTH OR KOOT ROOT. The root of *Saussurea Lappa* (Compositæ). In powder it is used for preserving furs, etc., from moth. The oil is used as a basis for perfumes: the powder for sachets.

**A Liquid Extract 1 = 1** made by percolation with 90% alcohol to exhaustion and concentrating. Used for the treatment of asthma:  $\frac{1}{2}$  to 2 drachms stated to stop paroxysms. It may be taken as such in a little water (to cut short a paroxysm), or in the form of a mixture, taken 3 to 4 times daily, containing potassium iodide or potassium bromide 5 to 10 gr., tincture of belladonna 3 to 5 m., borax 2 gr., liquid extract of *S. lappa*  $\frac{1}{2}$  to 2 dr., spirit of chloroform 10 m., water 1 oz., for continued administration. Has no cumulative action. Is not claimed to produce a permanent cure.—R. N. Chopra, *Indian med. Gaz.*, Apr., 1928, 189; *Indian J. med. Res.*, 1929, 351.

## ERGOTA

### B.P.

*Syn.* SECALE CORNUTUM (*U.S.P. XI*, *Fr. Cx.*, *P. Ital. V*, *P. Helv. V*, *P. Belg. IV*), ESPOLÓN DE CENTENO, CORNEZUELO DE CENTENO (*F.E. VIII*).

[P1] "Alkaloids, the following; their salts, simple or complex:—Ergot, alkaloids of."

"Ergot (the sclerotia of any species of *Claviceps*); extracts of ergot; tinctures of ergot."

[S1] "Alkaloids, the following; their salts, simple or complex:—Ergot, alkaloids of."

"Ergot; extracts of ergot; tinctures of ergot."

[85] "*Alkaloids—Ergot, alkaloids of—specify proportion as the proportion of any one alkaloid of ergot that the preparation would be calculated to contain on the assumption that all the alkaloids of ergot in the preparation were that alkaloid.*"

**Dose.**—The B.P. requires *Ergota Præparata* (*vide infra*) to be dispensed when *Ergota* is prescribed. *Fr. Cx.*, maximum single dose 15 grains; maximum during 24 hours 70 grains approximately.

The sclerotium of the fungus *Claviceps purpurea* (Pyrenomyces) on *Secale cereale* (Gramineæ). It contains not less than 0.05% of ergot alkaloids calculated as ergotoxine.

**Storage.** Ergot should be kept entire and not powdered. If powdered the fat should be removed immediately, otherwise the alkaloid content decreases.

**Antidotes.** Empty stomach by emetic or by stomach tube, using dilute solution of tannic acid. Keep patient lying down and warm. Give purgative dose of castor oil or magnesium sulphate. Medicinal charcoal has been recommended. Stimulants, *e.g.*, brandy,  $\frac{1}{2}$  oz., or aromatic spirit of ammonia,  $\frac{1}{2}$  dr., in water. Nitroglycerin sometimes used.

**Uses.** Ergot stimulates plain muscle throughout the body, but its use is confined almost entirely to obstetrics, owing to its action in exciting uterine contractions, and it is especially employed after delivery to check post-partum hæmorrhage. It is also used as an emmenagogue.

Because of its success in uterine hæmorrhage it has been widely employed in various other internal hæmorrhages, but its use in such conditions is irrational, and in the treatment of cerebral and pulmonary hæmorrhages its administration may actually be harmful.

**ENURESIS IN CHILDREN.** Ext. Ergot. Liq. 5 minims for a child of 5 years, with  $2\frac{1}{2}$  minims Ext. Glyc. Liq. and a drop of peppermint, effectual in a fortnight. Worth trying.—A. Patton, *Brit. med. J.*, ii/1930, 981.

[P1-81] **Ergota Præparata (B.P.).**

**Dose.**—5 to 15 gr. (0.3 to 1 g.); it may be given in a cachet or capsule.

Powdered and defatted ergot adjusted to contain 0.1% of ergot alkaloids calculated as ergotoxine. Probably the best ergot preparation for giving *per os*.

*P. Helv. V* requires the defatted powder to be used in dispensing and for preparing galenicals (unless the contrary is specified), the dose being reduced by 30%.

[P1-81] **Erbolin** (*Glaxo Laboratories, London*). A stable physiologically standardised preparation of powdered, defatted ergot in capsules, each containing the equivalent of 0.5 mg. ( $\frac{1}{200}$  grain) of ergotoxine.

[P1-81] **Extractum Ergotæ (B.P.C.).**

**Dose.**—1 to 3 grains (0.06 to 0.2 g.).

A soft extract containing when freshly prepared 0.5% of alkaloids; 3 gr. contain about  $\frac{1}{10}$  gr. of total alkaloids. The extract is much more stable than the liquid extract, its alkaloidal content

being practically unaltered after two years' storage under ordinary conditions.

[P1-S1] **Extractum Secalis Cornuti** (*P. Ital. V, F.E. VIII, P. Belg. IV*). *Syn.* EXTRACTUM CLAVICIPIS (*Fr. Cx.*), ERGOTINA BONJEAN, ERGOTIN.

*Dose.*—2 to 8 grains (0.12 to 0.5 g.).

An aqueous extractive precipitated by alcohol and evaporated.

[P1-S1] **Extractum Ergotæ Liquidum** (*B.P.*).

*Dose.*—10 to 20 minims (0.6 to 1.2 ml.).

Prepared from defatted ergot by percolation with a 1% solution of tartaric acid in alcohol 50%, and adjusted to contain not less than 0.06% *w/v* of total ergot alkaloids, calculated as ergotoxine, when freshly prepared. It loses activity on keeping, and the *B.P.* permits a decrease in alkaloidal content to 0.04%.

The extract contains the water-insoluble alkaloids such as ergotoxine in addition to the water-soluble ergometrine, and there is now a demand for ergot preparations containing less ergotoxine, but standardised on their ergometrine content. In consequence, the *B.P.* 1914 liquid extract is again in favour, and this preparation gives the results required when made from a high potency ergot of Spanish or Portuguese origin.

[P1-S1] **Extractum Ergotæ Liquidum** (*B.P. 1914*).

*Dose.*—10 to 30 minims (0.6 to 1.8 ml.).

Prepared by macerating crushed ergot 10, with water 50, for 12 hours. Strain, repeat the macerations with water 25, again strain, mix the liquids and evaporate to 7 parts. When cold, add alcohol 3.75 parts, set aside and finally filter.

[P1-S1] **Fluidextractum Ergotæ** (*U.S.P. XI*). *Average dose.*—30. minims (2 ml.).

The potency per millilitre is equivalent to not less than 0.5 mg. of ergotoxine ethanesulphonate. It is prepared by extracting defatted ergot with a menstruum consisting of 2 volumes of hydrochloric acid and 98 volumes of diluted alcohol (48.4 to 49.5% *v/v*) or by extracting ergot with the same menstruum and, after cooling to  $-14^{\circ}$ , removing the congealed fat by filtration. One ml. represents 1 g. of ergot; the liquid extract must not be diluted and it must conform in potency to the above standard when assayed biologically, using single comb White Leghorn cockerels.

[P1-S1] **Ergodex** (*British Drug Houses, London*). *Dose.*—10 to 30 minims (0.6 to 2 ml.). A stable liquid preparation containing the whole alkaloidal content of ergot, including the alkaloid ergometrine, and suitable for oral use.

[P1-S1] **Infusum Ergotæ Recens** (*B.P.C.*).

*Dose.*—1 to 2 ounces (30 to 60 ml.). 1 in 20.

The fresh infusion should be dispensed when Infusum Ergotæ is ordered.

[P1-S1] **Mist. Ergotæ** (*N.I.F.*). Liquid extract of ergot (*B.P. 1914*) 15 m., chloroform water to  $\frac{1}{2}$  oz.

[P1-S1] **Mistura Ergotæ Alkalina** (*St. M.H.*). Liquid extract of ergot 20 m., iron and ammonium citrate 15 gr., weak tincture of ginger 20 m., chloroform water to 1 oz.

[P1-S1] **Mistura Bromidi cum Ergota** (*C.H.W.*). Potassium bromide 10 gr., liquid extract of ergot 5 m., cinnamon water to 1 oz.

[P1-S1] **Mistura Ergotæ cum Ferro** (*C.H.W.*). Liquid extract of ergot 15 m., solution of ferric chloride 10 m., spirit of chloroform 10 m., infusion of calumba to 1 oz.

[P1-S1] **Mistura Ergotæ cum Strychnina** (*R.F.H.*). Liquid extract of ergot 30 m., quinine sulphate 3 gr., solution of strychnine hydrochloride 3 m., dilute phosphoric acid 20 m., chloroform water to 1 oz.

[P1-81] **Tinctura Ergotæ Ammoniata** (B.P.C.).

*Dose.*— $\frac{1}{4}$  to 1 drachm (2 to 4 ml.). 1 in 4 with 10% of dilute solution of ammonia.

A sample contained 0.02% of alkaloids.—*Pharm. J.*, i/1936, 342.

[P1-81] **Ergometrina** (B.P. Add. I). *Syn.* ERGONOVINE (N.N.R.), ERGOTOCIN, ERGOBASINE, ERGOSTETRINE.  $C_{15}H_{23}O_2N_3 = 325.2$ .

*Dose.*— $\frac{1}{100}$  to  $\frac{1}{50}$  grain (0.0005 to 0.001 g.); by intramuscular injection,  $\frac{1}{400}$  to  $\frac{1}{100}$  grain (0.00025 to 0.0005 g.); by intravenous injection,  $\frac{1}{800}$  to  $\frac{1}{400}$  grain (0.000125 to 0.00025 g.).

In colourless, hygroscopic crystals becoming coloured on exposure to air. Two forms occur; one has m.p.  $162^\circ$  to  $164^\circ$  (decomp.), and the other, obtained from acetone, has m.p.  $212^\circ$ . The low m.p. form is less stable than that with the higher m.p.

*For method of extraction, see Vol. II.*

**Soluble** readily in alcohol and acetone, sparingly soluble in benzene and chloroform, moderately soluble in water. The aqueous solution has a blue fluorescence and becomes brown on exposure owing to oxidation. Ergometrine differs from other ergot alkaloids in being soluble in water, and almost insoluble in chloroform.

The low m.p. form tends to pass into the high m.p. form on keeping, and the latter can also be obtained readily by crystallisation in the presence of a crystal of the high m.p. variety. The more stable form is less soluble, but both have the same specific rotation.—R. L. Grant and S. Smith, *Nature, Lond.*, i/1936, 154.

Stable solutions may be prepared by addition of ascorbic acid, 10 mg. per ml.—A. Solomon and R. W. Spanhoff, *Quart. J. Pharm.*, 1938, 652.

**Pharmacology.** Ergometrine differs from other ergot alkaloids by the absence of the paralysing effect on augmentor sympathetic actions, and by a much weaker activity in the production of gangrene. Its specific action is to initiate a long persistent rhythm of powerful contractions in a uterus normally quiescent, as in the puerperium. If the uterus already exhibits a vigorous spontaneous rhythm, ergometrine does not enhance it. It is more readily absorbed than ergotoxine, but anaesthetised animals differ from the human patient in showing no regularity of response to oral doses of ergometrine which produced immediate effects when given intravenously.

**Uses.** Clinically, it is remarkable for its rapidity of action, which distinguishes it from the ergotoxine-ergotamine group. By mouth, using average doses, an effect is usually seen in 5 to 8 minutes, by intramuscular injection in from 3 to  $4\frac{1}{2}$  minutes, and by intravenous injection in about 1 minute. The onset of action is abrupt and there is a well-marked uterine spasm lasting for about half an hour, after which strong isolated contractions occur at regular intervals and continue for 2 to 3 hours or more. When powerful action is required in the shortest possible time, larger doses should be employed, such as, by mouth, 1 mg.; intramuscularly, 0.5 mg.; intravenously, 0.125 mg., though these doses have been increased to as much as 1.5 mg., 0.75 mg., and 0.15 mg. respectively, without symptoms of intolerance. It is freer from

unpleasant side-effects (depression, headache, and nausea) than the ergotoxine-ergotamine group, and from dangerous gangrene-producing properties.

The greatest clinical value of ergometrine is in the treatment of post-partum hæmorrhage; it may be safely administered at the beginning of the third stage if necessary. It has also been found of value in the control of hæmorrhage following Cæsarean section. Many workers favour its use in the puerperal period for the promotion of involution and the prevention and control of sepsis, but its use in this connection has not been universally accepted. Varying results have also been obtained in the treatment of incomplete and inevitable abortion. It may be used as a palliative measure in certain cases of menorrhagia and metrorrhagia.

**[P1-81] Ergometrine Acid Tartrate.**

$C_{19}H_{25}O_2N_3, C_4H_6O_4 = 475.4$ . Colourless crystals, soluble in water.

**[P1-81] Basergin** (*Sandoz, London*). A stable preparation of ergobasine (ergometrine) tartrate. Supplied in tablets containing 0.00025 g., solution, 1 ml. = 0.00025 g., and ampoules, 1 ml. = 0.0002 g. *Dose*.—1 tablet or 15 to 30 drops of solution one to three times daily, or  $\frac{1}{4}$  to 1 ml. subcutaneously, intramuscularly, or intravenously, following the third stage of labour.

**[P1-81] Ergometrine Hydrochloride.** White crystals, soluble in water, m.p.  $245^\circ$  to  $246^\circ$  (decomp.).

**[P1-81] Ergotrate** (*Lilly, London*). Ergometrine maleate in tablets containing 0.2 mg. ( $\frac{325}{100}$  gr.).

**[P1-81] Ergotrate H.** Ergometrine hydracrylate in ampoules containing 0.2 mg. ( $\frac{325}{100}$  gr.) for intravenous injection.

**[P1-81] Ergotamine.**  $C_{33}H_{35}N_5O_5 = 581.6$ .

Colourless crystals darkening on exposure to light.

**Soluble** in alcohol 90%, chloroform and acetone, sparingly soluble in ether.

Its pharmacological action is similar to that of ergotoxine but it has a greater sympathicolytic effect. It is available commercially only as the tartrate in the proprietary article Femergin, *q.v.*

Some discussion has taken place between Prof. Stoll and Drs. Smith and Timmis as to the occurrence of ergotamine in ergot of rye, the English workers maintaining that ergotamine is not a normal constituent (*vide Lancet*, ii/1930, 652, 873, 994, 1148).

**[P1-81] Ergotamine Tartrate** is official in *P. Belg. IV* with formula  $(C_{33}H_{35}O_5N_5)_2, C_4H_6O_6, 2CH_3OH$ .

*Dose*.—0.001 g. two to four times daily; subcutaneously or intramuscularly, 0.00025 g.

**Toxic Effects.** Its continued use may give rise to symptoms of ergotism, and cases of gangrene have been reported.

Gangrene of the feet, necessitating amputation of the legs, following hypodermic injections of ergotamine tartrate in a fisherman suffering from toxæmia with jaundice of unknown origin, the injections being given for pruritus. 19 ml. was injected within a week. Oral use is less likely to produce toxic effects.—W. M. Yater and J. A. Cobill, *J. Amer. med. Ass.*, i/1936, 1635.

Report of a case of gangrene and death in a middle-aged woman following injections (four of 0.25 mg.) of ergotamine tartrate for pruritus.—S. E. Gould *et al.*, *J. Amer. med. Ass.*, i/1936, 1635.

A case of impending gangrene of both feet, due to arterial spasm following the administration of ergotamine tartrate, was almost immediately relieved by the intravenous and oral administration of papaverine hydrochloride. Initially  $\frac{1}{4}$  gr. was given intravenously in 1 ml. of normal saline, 6 hours later the same dose was given orally, and after a further 4 hours the intravenous dose was repeated. The pain was completely relieved within 12 hours.—S. Perlow and L. Bloch, *J. Amer. med. Ass.*, ii/1937, 27.

**Contraindications.** It should not be administered to pregnant women or during labour, neither is its use advisable in puerperal sepsis, severe toxæmia, arteriosclerosis and other vascular diseases.

**Uses.** Ergotamine tartrate is characterised by two main actions, namely, a powerful and prolonged action on the uterus, and paralysis of the sympathetic nerve endings. It is of value as a uterine hæmostatic and is indicated in obstetric and gynaecological hæmorrhages whenever prolonged action is desired. It has been widely employed in the treatment of migraine for the abortion of attacks, and has been advocated in Graves' disease and certain psychotic conditions.

**GRAVES' DISEASE.** Ergotamine tartrate injections, 1 mg. intramuscularly, gave improvement, but not in severe cases. Or subcutaneously  $\frac{1}{16}$  grain each morning, repeated in the evening if tolerated. Suspend for a week or two after 20 to 25 days.—*Per Prescriber*, 1929, 391.

**MIGRAINE** treated by ergotamine tartrate, 2 mg. daily by mouth, with additional 2 mg. when an attack is threatened.—*Per Prescriber*, 1929, 33.

Given in 45 cases (6 men and 39 women) it caused abrupt termination of headache in 40. Speed of pharmacological effect varies with route of administration, e.g., intravenously, relief in 15 to 30 minutes; subcutaneously, 1 to 2 hours; *per os*, 2 to 3 hours. Recommended single dosage 0.5 mg. subcutaneously or 1 mg. *per os*. Only give half subcutaneous dose at first trial. Injection can be repeated after 2 or 3 hours. For prompt sustained effect 0.25 mg. intravenously and at the same time the same amount subcutaneously.—W. G. Lennox, *New Engl. J. Med.*, 1934, 210, 1061.

Among the most recent and promising forms of treatment is the intramuscular injection of ergotamine tartrate 0.5 ml. The benefit as to headache is frequently almost dramatic, though it may cause vomiting or uterine colic. The usual effect is to bring promptly to a close an attack which would otherwise disable the patient for hours, or even days.—M. Critchley, *Brit. med. J.*, ii/1935, 795.

Intravenous or subcutaneous injections of 0.5 mg. of ergotamine tartrate gave relief in migrainous headaches in over 90% of patients, even in those which had proved resistant to other forms of treatment.—W. G. Lennox *et al.*, *Amer. J. med. Sci.*, ii/1936, 57.

Not only is ergotamine of little account in stopping non-migrainous headaches, but it may actually initiate a headache.—W. J. Lennox and co-workers, *per J. Amer. med. Ass.*, ii/1936, 906.

In five years' experience no serious complications have occurred in the treatment of 189 patients with migraine headache. Contraindications to the use of ergotamine tartrate are septic states, especially when associated with intravascular foci and obliterative vascular disease, especially when coronary. Treatment should be continued with caution in the presence of marked arteriosclerosis, hepatic or renal disease, vitamin C deficiency, and hypersensitivity to the drug. When correctly administered in the absence of contraindications, ergotamine tartrate may be considered a safe and extremely valuable means of aborting or terminating migraine headaches.—T. J. C. von Storch, *J. Amer. med. Ass.*, ii/1938, 293.

[P1-81] **Femergin** (*Sandoz, London*). GYNERGEN in U.S.A. Tablets contain 0.001 g. of ergotamine tartrate. Also supplied in solution for oral use and ampoules for injection.

[P1-81] **Neo-Femergin** (*Sandoz, London*). A preparation combining the persistent action of ergotamine with the rapid action of ergobasine (ergometrine). Supplied in tablets containing 0.000125 g. ergobasine tartrate and 0.00025 g.

ergotamine tartrate; also in solution and ampoules containing similar proportions. *Dose*.—1 tablet or 15 to 30 drops of solution three times daily, or  $\frac{1}{2}$  to 1 ml. subcutaneously or intramuscularly after expulsion of the placenta. Should not be given before or during labour.

[P1-81] **Ergotinina**. *Syn.* ERGOTININE CRYSTALLISÉE (*Fr. Cx.*).

$C_{23}H_{23}O_4N_2 = 609.7$ .

*Dose*.— $\frac{1}{100}$  to  $\frac{1}{50}$  grain (0.0003 to 0.001 g.). *Fr. Cx.* has the latter as *max. single dose*, and 0.002 g. as *max. daily dose*.

An alkaloid in minute colourless needles, soluble in 200 of alcohol 95%, less in ether, very soluble in chloroform, insoluble in water.

This alkaloid has been proved to be inert.

[P1-81] **Ergotoxina** (*B.P.C.*).

*Dose*.— $\frac{1}{100}$  to  $\frac{1}{50}$  grain.

A white amorphous powder darkening on exposure to light and air.

**Soluble** in alcohol, acetone, chloroform and ethyl acetate, also in benzene, from which it crystallises with 2 molecules of solvent; almost insoluble in water.

**Uses.** Ergotoxine causes contraction of plain muscle, particularly of the uterus. It is usually employed by injection in the form of the soluble salt ergotoxine ethanesulphonate, and may be employed in this manner to control hæmorrhage and counteract uterine atony and subinvolution after parturition in Cæsarean section. It should not be used during labour.

The degree of uterine spasm and its duration after permissible dosage is not so great as has sometimes been supposed. Repeated investigations have shown that, in the puerperal uterus at least, spasm does not last longer than about an hour and a half after 0.5 mg. of ergotoxine or ergotamine intramuscularly. —Chassar Moir, *Proc. R. Soc. Med.*, 1935, 1661.

[P1-81] **Ergot Aseptic Ampoules** (*Parke, Davis, London*). Preparation of ergot preserved with Chloretone; for intramuscular injection. *Dose*.—1 ml.

[P1-81] **Ernutin** (*Burroughs Wellcome, London*). A solution physiologically standardised for hypodermic use, containing ergotoxine, Tyramine and Ergamine (*v. infra*) in two forms: (*a*) for oral use, *dose*.—30 to 60 minims, to be given after labour is completed, every 3 hours until contraction effected, and (*b*) for hypodermic use, *dose*.—5 to 10 minims, after expulsion of the placenta.

[P1-81] **Ergotoxinæ Æthanosulphonas** (*B.P.*). Probable formula  $C_{28}H_{41}N_2O_6 \cdot C_2H_5 \cdot SO_2 \cdot OH = 737.5$ .

*Dose*.— $\frac{1}{100}$  to  $\frac{1}{50}$  grain (0.0005 to 0.001 g.) by subcutaneous or intramuscular injection.

Colourless, odourless, acicular crystals containing about 83.6% of ergotoxine.

**Soluble** in alcohol 90%; readily soluble in methyl alcohol, sparingly soluble in water.

[P1-81] **Ergothane** (*Evans, Sons, Lescher & Webb, Liverpool*). Ampoules of ergotoxine ethanesulphonate solution containing 0.0005 g. per ml. *Dose*.—0.5 to 1 ml. (0.25 to 0.5 mg.) intramuscularly or subcutaneously, repeated in 24 hours if necessary.

[P1-81] **Ergotoxinæ Phosphas** (*B.P.C.*).

*Dose*.— $\frac{1}{100}$  to  $\frac{1}{50}$  grain (0.0005 to 0.001 g.) by subcutaneous or intramuscular injection.

Colourless crystals darkening on exposure to air and light.

**Soluble** 1 in 18 of boiling alcohol 90%, less soluble in cold alcohol, sparingly soluble in water.

**Other Ergot Alkaloids.**

In addition to the above alkaloids, other constituents have from time to time been reported.

[P1-S1] **Sensibamine** was obtained in 1932. It is a molecular compound of two alkaloids, ergotamine and ergotaminine. It is less stable than ergoclavine, and, on solution in alcohol, ergotaminine crystallises out.

[P1-S1] **Ergoclavine** was obtained by W. Küssner (*Arch. Pharm., Berl.*, 1934, 503) in hygroscopic crystals, resembling sensibamine but differing from it in being recrystallisable from acetone or alcohol. It is stated to constitute 16 to 20% of the total alkaloids of Spanish and Russian ergots. Ergoclavine consists of an equimolecular compound of two alkaloids, which are probably ergosine and ergosinine.

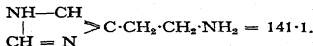
**Ergoclavine and Sensibamine** are pharmacologically identical with ergotoxine and therefore also with ergotamine.—A. Vartiainen, *J. Pharmacol.*, 1935, 54, 259.

[P1-S1] **Ergometrine**.  $C_{11}H_{15}O_2N_2$ . Obtained by S. Smith and G. M. Timmis (*Nature, Lond.*, ii/1934, 259). Has no physiological action, and bears the same relationship to ergometrine as ergotaminine to ergotamine, or as ergotamine to ergotoxine. It can be converted to ergometrine by treatment with acid.

[P1-S1] **Ergosine** and [P1-S1] **Ergosinine** are isomeric alkaloids, probably  $C_{11}H_{15}O_2N_2$ , which have been obtained also by Smith and Timmis (*Nature, Lond.*, i/1936, 111, 1075). The latter is sparingly soluble in water and methyl alcohol but can be recrystallised from aqueous acetone.

A new phenolic alkaloid, which does not give the blue colour with *p*-dimethylaminobenzaldehyde, has been isolated in extremely small yield. It contains one nitrogen atom, the probable formula being  $C_{11}H_{11}O_4N$ , and the name suggested is **Ergomonamine**.—G. W. Holden and G. R. Driver, *Quart. J. Pharm.*, 1936, 230.

**Histamine. Syn. and Prop. Name.** AMINOETHYLGLYOXALINE, 4- $\beta$ -IMINAZOLYLETHYLAMINE, ERGAMINE (*Burroughs Wellcome, London*).



A base present in ergot, usually prepared synthetically from protein decomposition products. It is used therapeutically as the acid phosphate.

**Pharmacology.** It has intense action on plain muscle. The plain muscle fibre of the uterus in particular is stimulated to contraction by minute doses. Injected subcutaneously it causes fall of blood pressure, and in other than minimal doses it produces a violent and intense erythema all over the body, headache, conjunctivitis, paræsthesias, vomiting, tenesmus, bronchial spasm and unconsciousness.

**Histamine in Relation to Blood Pressure.**

Histamine is, no doubt, liberated from the tissues in response to injury. Intravenously in cats a dose of 1 to 2 mg. per kilo causes respiratory disease, due to contraction of bronchiolar muscles, and rise of blood pressure, due to contraction of muscles of arterioles. Profound fall of blood pressure follows within 4 or 5 minutes. It has a powerful dilating effect on the smallest vessels. The hypothesis of "Histamine Shock" is that the circulation is brought to a precariously low point by depletion of the central vessels, much rich corpuscular blood remaining locked in the minute vessels and much of its fluid part finding its way into extravascular tissue spaces. Similar effects in man with small intravenous or subcutaneous doses. Larger doses subcutaneously (6 to 8 mg.) cause fall of blood pressure, respiratory distress, contraction of stomach, and occasionally collapse.—"The Blood Vessels of the Human Skin and their Responses," Thomas Lewis (1927), 108-109 (H. K. Lewis).

**Histaminæ Phosphas Acidus (B.P. Add. I). Syn.** HISTAMINÆ PHOSPHAS (*U.S.P. XI*).  $C_5H_9N_3 \cdot 2H_3PO_4 = 307.2$ .



**Dose.**— $\frac{1}{150}$  to  $\frac{1}{80}$  grain (0.0005 to 0.001 g.) by subcutaneous injection.

In colourless, odourless, prismatic crystals. **Soluble** 1 in  $4\frac{1}{2}$  of water, slightly in alcohol.

**Uses.** Is administered hypodermically, by inunction, and by ionisation in the treatment of rheumatism, being especially useful in chronic cases with vasomotor disturbances. Is also useful in chronic rheumatoid arthritis, in osteoarthritis and related conditions, and in pruritus associated with urticaria, and has been employed with success in Ménière's disease and in headache associated with vasodilatation. Its stimulating action on the production of gastric juice is used in the differential diagnosis of pernicious and secondary anæmias by means of the fractional test meal; in the achlorhydria of pernicious anæmia 0.5 to 1 ml. of 1 in 1000 solution does not induce secretion of hydrochloric acid. The 1 in 1000 solution has also been used in the diagnosis of circulatory disturbances such as Raynaud's disease. In normal patients, when the solution is pricked into the skin, a red spot followed by a weal should appear in about  $2\frac{1}{2}$  minutes. In Raynaud's disease and allied affections this reaction is delayed.

\* **ASTHMA.** With suitable technique and individualised dosage, histamine treatment may produce permanent and satisfactory results in bronchial asthma and urticaria. Begin in severe cases with 0.00001 mg. and in milder cases with 0.0001 mg. The first injection is given intracutaneously, and when it causes no noticeable reaction, give the same dose subcutaneously the following day, later injections given at intervals of two days. Doses gradually increased up to a maximum of 0.01 mg.—A. Dzsinič, *Klin. Wschr.*, ii/1935, 1612.

**CHEYNE-STOKES' RESPIRATION.** Normal breathing resumed and continued for about 6 hours after small dose of histamine subcutaneously. Slight headache, feeling of warmth, and occasional reddening of skin of arms and neck—symptoms pass off in an hour. Following two further injections next day Cheyne-Stokes' respiration ceased altogether.—F. Kisch, *Klin. Wschr.*, 1930, 1819, per *Prescriber*, 1930, 655.

**HEADACHE.** Of 85 patients suffering from a type of severe vascular headache associated with evidence of vasodilatation, 65 obtained definite permanent relief for periods of from 2 weeks to 18 months, following subcutaneous injection of 0.05 mg. of histamine twice daily on two consecutive days, increasing on the third day to 0.066 mg. twice daily, and then 0.1 mg. twice daily for two or three weeks.—B. T. Horton *et al.*, *Proc. Mayo Clin.*, 1939, 257.

**MÉNIÈRE'S DISEASE.** Eleven patients, all of whom were in the acute or subacute stages of the disease and were either partially or totally incapacitated, all responded to histamine intravenously in a spectacular manner. 1.9 mg. of histamine acid phosphate was given in 250 ml. of normal saline, the time taken to administer the solution being one and a half hours. In some cases the injection was repeated on two or three successive days. No ill effects resulted from the injections.—C. H. Sheldon and B. T. Horton, *Proc. Mayo Clin.*, i/1940, 17.

**POST-OPERATIVE COLLAPSE.** After the intravenous injection of 0.005 mg. of histamine most persons show a brief fall of the systolic blood pressure, whereas those subject to post-operative circulation disturbances react to such an injection with a fall of blood pressure followed by an often considerable rise. In these latter patients the subcutaneous injection of 0.5 to 1 mg. of histamine twice a day for 8 to 10 days before an operation has been found a valuable prophylactic measure to combat the tendency to post-operative collapse.—S. Rusznyak and co-workers, *Dtsch. med. Wschr.*, 1935, 1111.

**RHEUMATISM.** Histamine given subcutaneously in the form of a solution of strength of 1 mg. of histamine acid phosphate in 1 ml. of saline, with 0.5% of phenol. Initial dose 0.1 mg., increased daily by 0.05 mg. till definite improvement observed. Satisfactory dose usually between 0.1 and 0.5 mg., which is

repeated 2 or 3 times weekly and further increased if response diminishes. Sensitivity varies: women usually more sensitive than men (but does not affect menstruation). With long intervals between doses (e.g., a week) some increased sensitivity observed. Of benefit in all types of rheumatism, but in particular the type characterised by co-existence of impaired grip, the result of periarticular arthritis in the hand with vasomotor disturbances (e.g., cold and cyanotic fingers). Cases with gross heart disease or high blood pressure unsuitable. Patients lie down for 15 to 30 minutes after injection to diminish liability to headache and giddiness.—B. Shanson and C. G. Eastwood, *Lancet*, i/1934, 1226. See also F. S. Mackenna, *ibid.*, 1228, Bissett, *ibid.*, 1366, and Woodmansey and Bissett, *ibid.*, ii/1933, 1018, and references under Electrotherapy in Vol. II.

A useful treatment for the common complaint of morning stiffness (in chronic rheumatism) is to inject hypodermically 0.1 ml. of histamine acid phosphate in saline. The effect is to cause "unlocking" of the stiff joints and to increase the power of the hand grips. If found to suit, the dose may be increased gradually, and later, if improvement is maintained, the intervals between injections may be lengthened.—Whitla, 8th Edn., 1938.

#### Liquor Histaminæ Phosphatis (U.S.P. XI).

Average dose.—5 minims (0.3 ml.) by parenteral injection. A 0.1% solution of histamine acid phosphate in distilled water.

**Amino-Glaucosan** (*Saccharin Corporation, London*). 10% solution of histamine hydrochloride used in the form of eye drops as a miotic in acute glaucoma.

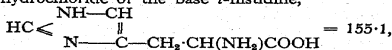
**Imadyl** (*Roche Products, Welwyn Garden City*). Histamine preparations in various forms—2% ointment for ionisation (may also be used by massage), also tablets containing 0.05 g. (1 tablet to 1 litre for immersion or 1 in 5000 solution for moistening anode pad); ampoules for injection, 1 mg. in 1 ml. (doses increasing from 0.1 to 0.5 mg.).

**Thio-Histamine** (*British Drug Houses, London*). An organic sulphur compound administered by intramuscular injection for the removal of fibrotic lesions resulting from previous inflammation. Also useful in acne rosacea and vulgaris, seborrhoeic and other forms of dermatitis, and in thrombo-angitis obliterans. It is similar to Contramine (*q.v.*) in therapeutic effects, but is quicker in action. A course of treatment consists of the injection on three successive days of 0.001 g., 0.002 g., and 0.003 g., no further injections being made for 6 to 8 weeks. The solution may also be applied locally around the lesion twice daily until signs of inflammation occur.

**Histaminase** is an enzyme, which specifically inactivates histamine. It is a compound of physiologic albuminoid substance obtained from the intestinal mucous membrane as a loose white powder, which is stable and dissolves in water to a slightly opalescent fluid. Since it has been shown that there is a release of a so-called H-substance in the blood during allergic shock, which is probably histamine, patients with various allergic cutaneous disorders were treated with histaminase. It was administered either intramuscularly or orally as enterically coated tablets containing five units, the unit being the amount necessary to inactivate 1 mg. of histamine during 24 hours incubation at 37° in a phosphate buffer solution at pH 7. Out of a total of 35 patients treated there was a partial or complete improvement in all but 9. Dosage has to be worked out for each individual case, but it is recorded that no untoward reactions were noted after patients had taken as much as 150 histamine-detoxifying units daily for four or five days. Patients receiving intramuscular injections had very much better results than those receiving the enzyme in tablet form, although the first four injections elicited symptoms comparable to those following protein shock therapy.—Goldberg, *J. Amer. med. Ass.*, ii/1940, 429.

#### Histidine Hydrochloride.

Dose.—3 grains (0.2 g.), in 4% aqueous solution, given daily for about 3 weeks by subcutaneous or intramuscular injection. The monohydrochloride of the base *L*-histidine,



which is the amino-acid corresponding to histamine.

The 4% solution is administered by injection in the treatment of peptic ulcer, and it is claimed that symptomatic improvement occurs after 4 or 5 injections. The theoretical basis of the treatment rests on the work of Aron and Weiss (*Pr. méd.*, 1933, 93, 1880), who showed that peptic ulcer could be produced in dogs by preventing duodenal digestion by surgical means. They suggested that ulcer formation was connected with a deficiency of amino-acids and that this deficiency was corrected by the injection of histidine. These experiments were subjected to serious criticism by H. C. Barry and H. W. Florey (*Lancet*, ii/1936, 728) who, as a result of further experiments on cats and pigs, were unable to substantiate the suggestion of Aron and Weiss. In general, it may be said that the extremely favourable results reported by early investigators have not been borne out by more recent experimental and clinical research, but that the drug may be found of value in selected cases as an adjunct to the diet-alkali régime.

Disappointing relapses are known, and there will probably be general agreement that histidine is not a specific remedy for peptic ulcer, in the sense that it does not counteract the cause. If this is so, it must seem unwise to relax attention to dietetic and general measures while carrying out injection treatment. The longest case-histories hitherto reported are less than two years, and the word "cure" is therefore inappropriate to any of them. The time has not yet come for accepting an entirely new theory of ulcer causation and for abandoning the ordinary rules of diet and management.—*Lancet*, i/1936, 95.

Results obtained in 40 patients do not warrant routine injections of histidine in all ulcer patients. The expense involved, the 24 consecutive intramuscular injections, the mild reactions experienced by an appreciable number of patients, the high percentage of recurrences within 6 months after treatment, and the fact that approximately the same percentage of patients respond favourably to the diet-alkali regimen without histidine injections—these speak against the routine use of histidine in ulcer therapy. Histidine produced remission of ulcer symptoms in 55% of the patients treated; it did not prolong the symptom-free interval nor did it prevent recurrences; 85% of the patients who developed remissions have returned with ulcer symptoms within 6 months after treatment. However, histidine may be used as "extra artillery" in patients not responding to the diet-alkali-antispasmodic management. About 50% of the latter patients may thereby become symptom-free and an additional 20% moderately improved.—D. J. Sandweiss, *J. Amer. med. Ass.*, i/1936, 1459.

Comparison of a series of 41 cases treated with histidine hydrochloride with 40 controls treated with the usual diet-alkali ulcer regimen showed that symptomatic and radiologic response of the patients in the histidine series was not quite as good as that in the diet-alkali series, in either the initial or the sustained effects. The clinical improvement appears to be symptomatic and transient. Chronicity and rhythmicity is a characteristic feature of peptic ulcer. Histidine appears to have no effect other than to alter the rhythm slightly. It showed no constant effect on the hydrochloric acid secretion. The therapeutic indications for histidine in the treatment of peptic ulcer are necessarily limited. The extravagant claims that have been made for this substance are unwarranted.—D. A. Kirby (for Council on Pharmacy and Chemistry of the A.M.A.), *J. Amer. med. Ass.*, i/1936, 1472.

The treatment should be reserved for simple uncomplicated cases, for cases of stoma-ulcer, and in patients in whom other methods have failed. It should be regarded at present as an adjunct to simple diet-alkali treatment; it is most useful as an ambulatory method, but adequate after-treatment should be enforced on the usual lines.—E. Bulmer, *Lancet*, ii/1936, 734.

There can be no great objection to the use of histidine in addition to the usual treatment by rest and dieting, but its use as a substitute for the proper treatment is quite unjustifiable, as although an occasional patient may be saved trouble in this way, the majority will be placed in a fool's paradise, in which the ulcer, although temporarily latent, becomes progressively less amenable to treatment.—A. F. Hurst, *Practitioner*, ii/1936, 415.

Histidine not only lacks specificity but is no more beneficial than the injection of sterile water in the therapy of peptic ulcer.—R. Upham and H. Barowsky, *J. Amer. med. Ass.*, ii/1937, 422.

Injections of distilled water produced similar results to histidine. Remissions produced by histidine may be explained as psychic effects, added confidence in "something new" instead of the same "diet and powders." The symptom-free interval is longest after diet-alkali treatment. The short duration of remission and the high percentage of recurrences after parenteral therapy probably result because of more rapid increase in diet. In the present state of our knowledge all we can hope to accomplish by any form of ulcer therapy is to relieve symptoms, to delay relapses and to prevent complications. The parenteral method is not indicated in the routine treatment of peptic ulcer. It may be used only in those patients not responding to the diet-alkali régime, and only in association with, but not in place of, the usual planned diet. Unable to corroborate the experimental work of Aron and Weiss.—D. J. Sandweiss, *J. Amer. med. Ass.*, i/1937, 700.

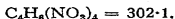
**Larostidin** (Roche Products, Welwyn Garden City) and **Stellidin** (Pharmaceutical Specialities (May & Baker) Ltd., London) are sterile 4% solutions of l-histidine hydrochloride in 5 ml. ampoules for intramuscular or subcutaneous injection. The former is also issued in tablets containing 0.2 g.

**Tyramina.** *Syn. and Prop. Name.* p-HYDROXYPHENYLETHYLAMINE, TYRAMINE (Burroughs Wellcome, London).  
 $\text{OH} \cdot \text{C}_6\text{H}_4 \cdot \text{CH}_2\text{CH}_2\text{NH}_2 = 137.1$ .

*Dose.*— $\frac{1}{4}$  to  $\frac{3}{4}$  grain (0.02 to 0.04 g.) by hypodermic injection of the acid phosphate.

An organic base present in aqueous extracts of ergot but obtained synthetically. Has a weak but prolonged adrenaline action but no local vasoconstrictor effect. It has practically no effect on the uterus. Has been used to raise blood pressure in collapse.

## ERYTHRITYLIS TETRANITRAS



*Syn.* ERYTHROL TETRANITRATE, NITRO-ERYTHRITE, ERYTHRO-TETRANITRAL, ERYTHROL NITRATE.

[P1] "*Erythrityl tetranitrate.*"

*Dose.*— $\frac{1}{4}$  to 1 grain (0.015 to 0.06 g.), increased to 3 grains or more in tablet form *vide infra*. When erythrityl, or erythrol, tetranitrate is prescribed, twice the prescribed amount of diluted erythrityl tetranitrate must be dispensed.

In colourless and slightly tar-like smelling crystals, m.p. 61°, formed by dissolving erythrol (a sugar obtained from various lichens, e.g., *Rocella tinctoria*, *R. fuciformis*, etc.), in fuming nitric acid, and precipitating by sulphuric acid. The crystals are explosive unless mixed with an inert diluent.

**Soluble** in water about 1 in 20,000, about 1 in 60 of absolute alcohol.

**Uses.** As a vasodilator. Its slight solubility as against that of glyceryl trinitrate (1 in 800) renders its action in reducing blood pressure slower and more prolonged. It is employed in angina pectoris, chronic Bright's disease, nephritis, aneurism, arteriosclerosis, Raynaud's disease, dyspnoea, headache and nervous

affections accompanied by high blood pressure. It is often effective in the paroxysms of asthma, especially if followed by a hot drink, and in relieving the spasms of lead colic. For angina, to avert paroxysms, even half a drachm a day has been taken. Præcordial pains are promptly relieved by one tablet 3 times a day.

Daily use of the tablets, beginning with  $\frac{1}{2}$  grain thrice daily and gradually increasing, will ward off attacks. Cumulative effect or tolerance has not been observed. Erythrityl tetranitrate produces little effect until half an hour after its administration, and the maximum effect is produced at the end of an hour; the arterial tension gradually increases again, but it does not return to its previous condition until about 10 hours after the dose has been taken.

**PRURITUS.** Of 21 cases of generalised pruritus, complete relief was obtained in 10 and moderate relief in 7 by the use of erythrityl tetranitrate by mouth in doses of 0.03 g. and glyceryl trinitrate in tablets containing 0.0006 g. Effect possibly associated with dilatation of the cutaneous vessels. Of no value in localised pruritus.—Prinzmetal, *Arch. Derm. Syph., N.Y.*, 1934, 843.

[P1] **Erythritylis Tetranitras Dilutus** (B.P., U.S.P. XI). *Syn.* ERYTHRITYL TETRANITRATE (50%), ERYTHROL TETRANITRATE (50%).

*Dose.*— $\frac{1}{2}$  to 2 grains (0.03 to 0.12 g.) representing  $\frac{1}{2}$  to 1 grain (0.015 to 0.06 g.) of pure erythrityl tetranitrate. U.S.P. average dose (of dilution)  $\frac{1}{2}$  grain (0.03 g.).

A mixture of approximately equal weights of erythrityl tetranitrate and lactose, the latter being added in order to minimise the risk of explosion.

[P1] **Tabellæ Erythritylis Tetranitratidis Diluti** (B.P.C.).

Contain 1 gr. (0.06 g.) in chocolate basis.

[P1] **Mannitylis Hexanitratis.** *Syn.* HEXANITRIN, NITROMANNITE, MANNITOL NITRATE.  $\text{CH}_2\cdot\text{ONO}_2\cdot(\text{CH}\cdot\text{ONO}_2)_4\text{CH}_2\cdot\text{ONO}_2=452.1$ .

*Dose.*— $\frac{1}{2}$  to 1 grain (0.016 to 0.06 g.) increased.

The nitrate of the hexahydric alcohol, mannite,  $\text{C}_6\text{H}_8\cdot(\text{OH})_6=182.1$ . In light acicular crystals, m.p.  $113^\circ$ , practically insoluble in water. Is used similarly to erythrityl tetranitrate but is more explosive and requires extra care. In angina and asthma its action is not so powerful, but probably more prolonged.

## EUONYMUS

B.P.C., *Fr. Cx.*

The dried root-bark of *Euonymus atropureus* (Celastraceæ), the wahoo or spindle-tree.

*Uses.* Possesses tonic, hydragogue cathartic, diuretic and anti-periodic properties.

**Elixir Euonymi et Pulsatillæ** (B.P.C.).

*Dose.*—1 to 4 drachms (4 to 16 ml.).

Tincture of euonymus 12.5, tincture of pulsatilla 12.5, simple elixir to 100.

R\*

**Extractum Euonymi (B.P.C.).** *Syn.* EUONYMIN.

*Dose.*—1 to 2 grains (0.06 to 0.12 g.).  $\frac{1}{4}$  to 1 grain cholagogue, 1 to 4 grains cathartic.

A brown alcoholic extractive containing calcium phosphate to keep it as powder. In commerce chlorophyll is sometimes added. *Fr. Cx.* has Euonymine Brune, *max. single dose*,  $1\frac{1}{2}$  grains. 1 grain, combined with 4 grains of iridin, is a successful purge.

**Extractum Euonymi Liquidum.**

1 = 1, made with alcohol (90%) 4, water 1. *Dose.*—10 to 60 minims (0.6 to 4 ml.).

**Liquor Euonymini et Iridini (B.P.C.).**

*Dose.*— $\frac{1}{4}$  to 1 drachm (2 to 4 ml.).

Contains the equivalent of about 3.5% w/v of extract of euonymus and 2% w/v of extract of iris.

**Liquor Euonymini et Pepsini (B.P.C.).**

*Dose.*— $\frac{1}{4}$  to 1 drachm (2 to 4 ml.).

Contains 1 gr. of extract of euonymus and 2 gr. of pepsin in 1 dr.

**[P1] Pilula Euonymini.**

Euonymin 2 gr., extract of hyoscyamus  $\frac{1}{4}$  gr., for 1 pill; taken at bedtime. A cholagogue stimulant, producing no depression or headache; requires to be followed by a saline aperient in the morning.

**Tinctura Euonymi (B.P.C.).**

*Dose.*—10 to 40 minims (0.6 to 2.6 ml.). 1 in 5 of alcohol 45%.

**Iridis Rhizoma (B.P.C., P. Helv. V).** *Syn.* ORRIS ROOT. The rhizome of *Iris germanica*, *I. pallida* and *I. florentina* (Iridaceæ). Contains "concrete oil of orris" or "butter of orris" (0.1 to 0.2%), used in perfumery, and irone,  $C_{15}H_{20}O$ , an oil with pungent odour, violet-like in very high dilution. Irone for use in perfumery is prepared synthetically from citral.

*Iris (B.P.C.), syn. BLUE FLAG*, is the dried rhizome and roots of *I. versicolor*, and contains a cathartic resinoid.

**Extractum Iridis (B.P.C.).** *Syn.* IRIDIN.

*Dose.*—1 to 3 grains (0.06 to 0.2 g.) in pills, often with extract of hyoscyamus or euonymus. A dry extract prepared with alcohol 70%, and mixed with calcium phosphate to reduce caking.

**EXTRACTUM FELLIS BOVINI***B.P.**Syn.* FEL BOVINUM PURIFICATUM.

*Dose.*—5 to 15 grains (0.3 to 1 g.) in enteric-coated capsules or pills.

A dark yellowish-green, bitter-sweet mass.

**Soluble** in water and alcohol 90%, insoluble in ether.

**Manufactured** by evaporating 20 of fresh ox bile to 5, mixing with 10 of alcohol 90%, separating the precipitate and evaporating the clear fluid to thick extract consistence. It is composed of bile salts, cholesterin, lecithin and bile pigments.

**Uses.** Bile plays an important part in the digestion, especially of the fatty acids, and is a powerful stimulant to the secretory activity of the liver. Ox bile has been usefully employed in a variety of conditions in which there is a diminution of bile in the

intestinal tract, *e.g.*, in catarrhal cholangitis and sluggish liver. By stimulating intestinal peristalsis it is also valuable in chronic constipation and for the removal of impacted fæces. For this latter purpose and for the treatment of paralytic ileus it has been employed in the form of an enema consisting of a 5% *w/v* solution of the extract in 5% soft soap solution, in doses of 5 to 20 ounces, or a 25% solution of fresh ox bile in hot water in doses of 1 to 4 ounces.

**ACUTE ILEUS.** Human bile used successfully in 9 out of 13 cases. Freshly secreted human bile from a cholecystectomy preferable, but can be kept in an ice-chest for a week. Give 2 oz. of bile in 4 oz. of saline per rectum and repeat every 4 hours until definite improvement is seen and bowels have been opened, reverting to bile if vomiting returns. Causes no discomfort and no difficulty in retention. Only water, orange juice, and glucose allowed until ileus is overcome. Both ox bile and vomited human bile have also been used, but both cause acute pain and are not so effective as fresh human bile.—R. St. Leger Brockman, *Lancet*, ii/1927, 320.

**Acute intestinal obstruction.** The action of human bile often dramatic.—*Lancet*, i/1929, 442.

**Extractum Fellis Bovis (U.S.P. XI).** *Average Dose.*—6 grains (0.4 g.). A dry extract adjusted with starch so that 1 g. represents 8 g. of ox bile.

**Extractum Bilis Bovis Depuratum (Fr. Cx.).** Shake 1000 g. of filtered ox bile with 1000 g. of alcohol (90%), and allow to stand 2 days. Filter, wash the residue with 200 g. of alcohol (70%), mix the filtrate and washings and evaporate below 50° to a firm extract.

**Fel Bovinum Exsiccatum.** *Dose.*—5 to 10 grains in cachets.

**Fel Bovis (U.S.P. XI)** is the fresh bile of the ox.

**Sodii Tauroglycocholas (B.P.C.).** *Syn.* BILE SALTS.

*Dose.*—2 to 6 grains (0.12 to 0.4 g.), preferably in capsules.

A yellowish-brown hygroscopic powder consisting chiefly of sodium taurocholate,  $C_{26}H_{44}O_7NSNa$ , and sodium glycocholate,  $C_{26}H_{42}O_6NNa$ . *Soluble* 2 in 1 of water, and in alcohol, insoluble in ether. It is prepared by extracting pig or ox bile with dehydrated alcohol, decolorising, and precipitating with ether. Is cholagogue, and assists pancreatic digestion. A 1% solution in water containing oil of eucalyptus 5%, is used for pediculosis.

The total salts of ox bile consist of a mixture of the sodium salts of taurocholic acid and glycocholic acid with small proportions of the sodium salts of tauro- and glyco-deoxycholic acids and tauro- and glyco-choleic acids. Taurocholic acid is a compound of cholic acid with the base taurine  $CH_3(NH_2) \cdot CH_2SO_3H$ , whilst glycocholic acid is a compound of cholic acid and glycine  $CH_2(NH_2) \cdot COOH$ . Similar compounds are formed by these bases with deoxycholic acid and choleic acid. The latter is a compound of deoxycholic acid and stearic or palmitic acid.—N. Evers and W. Smith, *Quart. J. Pharm.*, 1940, 213.

**Sodii Desoxycholas.**  $C_{24}H_{39}O_4Na = 414.3$ . Obtained from the tauroglycocholate by alkaline hydrolysis and crystallisation from glacial acetic acid of the separated bile acids. A white soluble powder, very irritating when inhaled. Bile salts appear to possess a solvent action on pneumococci, also on amœbæ and spirochætes. The addition of quinine enhances the action.

**SPRAY SOLUTION.** Sodium desoxycholate 4, quinine hydrochloride 0.5, glycerin 25, water to 100. For septic throats.

**TABLETS.** Contain sodium desoxycholate 1 gr., quinine ethyl carbonate  $\frac{1}{2}$  gr., peppermint oil  $\frac{1}{10}$  m., ammoniated glycyrrhizin 2 gr. Also made with acriflavine 1 in 1000. For infected throats.

**Sodii Glycocholas.**  $C_{26}H_{42}O_6NNa = 487.3$ .

*Dose.*—2 to 6 grains (0.12 to 0.4 g.).

A similar salt prepared from the lead salt precipitated from a tauroglycocholate solution by lead acetate. *Soluble* 1 in 2 of water and 1 in 3 of alcohol 90%. Appears to be a useful cholagogue for congestion of the liver, gall-stones, constipation and melancholia.

These salts produce slight fall of blood pressure, the taurocholate more than the glycocholate.

**CHOLECYSTITIS.** Sodium glycocholate 3 gr. with hexamine 7 gr. in cachets, 1 night and morning.—W. Bain, *Lancet*, i/1929, 495.

**MIGRAINE.** Good results in 22 patients following use of bile salts, capsules of sodium glycocholate being given in doses of 2 to 20 gr. *t.d.s.*, investigations showing that many cases of migraine are caused through errors of the biliary mechanism.—T. C. Hunt, *Lancet*, ii/1933, 279.

**Sodii Taurocholas.**  $C_{26}H_{44}O_7NSNa = 537.4$ .

*Dose.*—2 to 6 grains (0.12 to 0.4 g.), in pill, keratin-coated to prevent solution until it reaches the bowels.

A whitish powder, separated from the filtrate of the precipitation of tauroglycocholate with lead acetate. *Soluble* about 2 in 1 of water. It has been recommended for gouty obesity and dyspepsia.

**Lotio Sodii Taurocholatilis (B.V.H.).** Sodium taurocholate 1½ dr., oil of eucalyptus 1 oz., water to 20 oz. For pediculosis. The taurocholate emulsifies the oil and assists penetration of the louse's egg.

**Dehydrocholic Acid.** *Prop. Name.* DECHOLIN (*Riedel-de Haen, Berlin; Endocrines-Spicer, Watford*) (0.25 g. tablets).

$C_{24}H_{34}O_5 = 402.5$ .

*Dose.*—4 to 8 grains (0.25 to 0.5 g.).

Dehydrocholic acid is an oxidation product of cholic acid derived from the natural bile acids. It exists as an odourless, crystalline powder with a bitter taste. M.p. 233° to 235°.

Slightly *soluble* in alcohol and glacial acetic acid.

**Uses.** A potent cholagogue for use in functional hepatic insufficiency and for the prevention and treatment of migraine associated with faulty hepatic functioning. It is also of value for outlining the bile ducts at operation and to avert some of the post-operative complications; in cholecystography it accelerates the appearance of the gall-bladder shadow and hastens removal of the residual dye from the bile tract.

**Sodium Dehydrocholate.** *Prop. Names.* DECHOLIN SODIUM (*Riedel-de Haen, Berlin; Endocrines-Spicer, Watford*) (Ampoules contain 10 ml. of 20% solution), SUPRACHOL (*Richter, London*) (Ampoules contain 10 ml. of 5 or 20% solution; tablets 4 gr.).

*Dose.*—5 to 10 ml. of a 20% solution.

Sodium dehydrocholate is a colourless, crystalline powder with a bitter taste.

*Soluble* in water and alcohol; the aqueous solution is neutral to litmus.

**Uses.** This is employed for similar purposes to the above where more prompt action is required. It is administered intravenously,



one injection being given on each of three successive days, the first of 5 to 10 ml., and the second and third of 10 ml. each. It may also be employed to determine the rate of circulation of the blood. 10 ml. of the 20% solution is injected quickly intravenously. The time taken from the injection to the appearance of a bitter taste in the mouth is taken as that of the complete circuit. The normal circulation time is 10 to 17 seconds; in heart failure it is 23 to 40 seconds. To distinguish between right and left ventricular failure, 5 m. of ether may be injected to record the arm-to-lung time; this figure (normal 4 to 8 seconds) subtracted from the sodium dehydrocholate reading gives the pulmonary circulation time (normal  $4\frac{1}{2}$  to 10 seconds).

While sodium dehydrocholate has some diuretic effect it becomes a satisfactory diuretic in most cases only when combined with Salyrgan. The effective dosage of Salyrgan seems to be considerably lower when used in this combination, the maximum output following administration of 1 ml. or less of Salyrgan with simultaneous intravenous injection of 10 ml. of 20% sodium dehydrocholate. Sodium dehydrocholate intravenously is contraindicated in mechanical obstruction of the bile passages, acute hepatitis and acute yellow atrophy.—F. A. Weigand, *J. Amer. med. Ass.*, ii/1935, 2034.

**EXPERIMENTALLY INDUCED JAUNDICE.** As the result of the observation that attacks of severe jaundice confer complete relief from rheumatic symptoms in patients suffering from chronic atrophic arthritis and primary fibrositis, H. E. Thompson and B. L. Wyatt induced a condition of "therapeutic jaundice" in ten patients by means of intravenous injections of bilirubin and bile salts. A solution containing 10 mg. per kilo of bilirubin with 40 mg. per kilo of sodium dehydrocholate was employed, and the number of daily injections necessary to induce severe jaundice varied from seven to eleven. The first observable icterus in the eyes was noted after the first to fourth injection, and as a rule the icterus became progressively more marked with each succeeding injection. General reactions were of short duration and never appeared dangerous, and the observable jaundice disappeared in from 14 to 23 days after the last injection. Analgesia was noted after one to seven injections, the shortest period being twelve days; five of the ten patients have had no return of pain up to the present, the longest elapsed interval being a period of 5½ months.—Report of Fourth Ann. Meeting of the American Rheumatism Association, *J. Amer. med. Ass.*, ii/1937, 1482; P. S. Hench, *ibid*, 1481.

### SOME PROPRIETARY BILE SALT PREPARATIONS

**Bilisalin** (*Endocrines-Spicer, Watford*). Tablets contain bile salts 4 gr., and hepatic substance 2 gr. *Dose*.—One tablet 4 times daily for 3 days, double dose for 3 days, treble dose for 3 days, and continue until free bile appears in stool. In hepatic insufficiency, gall-stones, mucous colitis, etc.

**Cholalic** (*Allen & Hanburys, London*). An elixir of bile salts. Each drachm contains 1 gr. each of sodium taurocholate and sodium glycocholate. *Dose*.—1 to 3 teaspoonfuls. Constipation associated with hepatic deficiency.

**Degadol** (*Riedel-de Haen, Berlin; Endocrines-Spicer, Watford*). Desoxycholic acid and menthol in  $1\frac{1}{2}$  gr. tablets for diseases of the liver and biliary tract. *Dose*.—1 or 2 tablets thrice daily.

**Desibyl Capsules** (*Parke, Davis, London*). Desiccated bile in capsules each equivalent to about 2 to 5 ml. of fresh bile. Advocated as a cholagogue and choleric, and for use in the treatment of anorexia, intestinal indigestion and constipation. It is also advocated in steatorrhea for promoting intestinal absorption of fatty acids and fat-soluble vitamins. *Dose*.—2 or 3 capsules three times daily after meals. The capsules should be taken on a full stomach.

**Felagol** (*Richter, London*). Tablets containing sodium cholate 2 gr., hexamine salicylate  $2\frac{1}{2}$  gr., benzyl succinate  $\frac{1}{2}$  gr., lactic ferments  $\frac{1}{2}$  gr., oil of peppermint  $\frac{1}{2}$  gr. *Dose*.—2 tablets thrice daily.

**Felamine** (*Sandoz, London*). Hexamine glycocholate in tablets containing 5 gr. (0.3 g.). Cholagogue and biliary antiseptic. In catarrhal jaundice, constipation and enteritis and in the after-treatment of typhoid fever and for gall-stones.

**Glandulax** (*Richter, London*). Tablets of biliary salt, pancreas, duodenum, digestive ferments, pectin and aloin. *Dose*.—2 to 3 daily.

**Glanfel Tablets** (*Armour, London*). Enteric-coated tablets of 1 and 3 gr. consisting chiefly of sodium glycocholate and sodium taurocholate in the proportions existing in fresh bile. *Dose*.—One tablet one to three times daily. In indigestion, constipation, colitis, etc.

**Lactobyl** (*Continental Laboratories, London*). Tablets containing biliary salts, intestinal glands, hyperactivated charcoal, lactic ferments and extract of laminaria.

**Oleoformine** (*Corbière, Paris; Anglo-French Drug Co., London*). Combination of cholic acid, sodium oleate and hexamine in gluten-coated tablets. *Dose*.—3 to 4 tablets twice daily in acute cases; 2 tablets twice daily in chronic cases.

**Opobyl** (*Bengué, London*). Contains hepatic and biliary extracts, extracts of boldo and combretum, podophyllin and euonymin. For hepatic and biliary insufficiency.

**Pancrobilin** (*Reed & Carnrick, New Jersey; Coates & Cooper, London*). Pills (or liquid) containing pancreatic enzymes and bile salts. [P1-81] **Compound pills** contain in addition  $\frac{3}{32}$  gr. of strychnine,  $\frac{1}{16}$  gr. of belladonna and  $\frac{1}{2}$  gr. of aloin.

**Procholon Tablets** (*Squibb, New York; Savory & Moore, London*). Dehydrocholic acid tablets. *Dose*.—1 or 2 tablets two or three times daily. Hepatic insufficiency, cholecystitis, chronic constipation, etc.

**Sal-Cholate** (*Lilly, London*). Tablets containing sodium glyco- and taurocholate  $\frac{1}{2}$  gr., sodium salicylate  $1\frac{1}{2}$  gr., phenolphthalein  $\frac{1}{8}$  gr., extract of cascara sagrada  $\frac{1}{2}$  gr. *Dose*.—1 or 2 at bedtime or 1 after each meal.

**Salvacid** (*Coates & Cooper, London*). "Glycocholacetate, Thuryon" (ox bile derivatives combined with the antispasmodic principle of sage) 0.20 g., parathyroid extract 0.0001 g., sodium bicarbonate 0.05 g., calcium carbonate 0.05 g.

**Veracolate** (*W. R. Warner, London*). Tablets containing sodium glycocholate  $\frac{1}{2}$  gr., sodium taurocholate  $\frac{1}{2}$  gr., extract of cascara 1 gr., phenolphthalein  $\frac{1}{8}$  gr., oleoresin of capsicum  $\frac{1}{32}$  gr.

**Boldo** (*B.P.C., Fr. Cx.*).

*Dose*.—1 to 3 grains in cachet or capsule. The dried leaves of *Peumus Boldo* (*Monimiaceæ*) from Chili and Bolivia. They resemble those of Sweet Gale (*Myrica Gale*), but are more aromatic. In dyspepsia, liver affections, rheumatism, and as a diuretic for atony of the bladder.

**Tinctura Boldo** (*B.P.C.*). 1 in 10 of 60% alcohol.

*Dose*.—10 to 30 minims (0.6 to 2 ml.).

**Boldine Houdé** (*Laboratoires Houdé, Paris; Wilcox, JozEAU, London*). Granules containing 1 mg. of the alkaloid boldine. *Dose*.—3 to 6 granules daily. In hepatic disorders.

## FERRUM

Fe = 55.84.

**Ferrum** (*B.P.*). Consists of iron wire of 0.1 mm. diameter. *U.S.P. XI* requires it to be in form of fine bright wire, filings, or powder. *Fr. Cx.* includes filings (*Limaille de Fer*).

**Extractum Ferri Pomatum** (*P.G. VI, P. Ital. V, P. Jap. V*) is prepared by digesting iron filings in juice of sour apples, and contains 5% of iron.

**Tinctura Ferri Pomata** (*P.G. VI*). *Dose*.—15 to 30 minims (1 to 2 ml.). Ferrated extract of apples 1 part, cinnamon water (*P.G. VI*, containing 10% of alcohol) 9 parts.

**Liquor Ferri Acetatis.**

*Dose.*—5 to 15 minims (0.3 to 1 ml.).

Prepared by dissolving freshly precipitated ferric hydroxide in acetic acid and diluting with glycerin and water.

Pneumonia has been treated with full doses every 6 hours until crisis past.

**Solutio Ferri Subacetatis** (*P. Helv. V*) is a similar preparation adjusted to contain 5% of Fe.

**Liquor Ferri et Ammonii Acetatis.**

*Average dose.*—4 drachms (15 ml.).

Tincture of ferric chloride 4, dilute acetic acid 6, solution of ammonium acetate 50, aromatic elixir 12, glycerin 12, water to 100. To be freshly made. Useful in anæmia and particularly in chronic parenchymatous nephritis. It acts as a diuretic and diaphoretic.

**Mist. Ferri Acet. (N.I.F.).**

Strong solution of ammonium acetate 10 m., solution of ferric chloride 10 m., glycerin 10 m., water to  $\frac{1}{2}$  oz.

**Mistura Ferri Acetatis (W.H.).** *Syn.* BASHAM'S MIXTURE.

Solution of ferric chloride 15 m., solution of ammonium acetate 2 dr., dilute acetic acid 15 m., glycerin 15 m., water to  $\frac{1}{2}$  oz. For chronic parenchymatous nephritis.

**Ferrum Redactum** (*B.P., U.S.P. XI, Fr. Cx.*). *Syn.* QUEVENNE'S IRON.

*Dose.*—1 to 10 grains (0.06 to 0.6 g.). *U.S.P. XI* average dose 8 grains.

Fine powdered iron containing at least 80% (*U.S.P.* and *Fr. Cx.* 90%) of metallic iron, prepared by reducing ferric oxide with hydrogen.

*P. Dan.* and *P. Helv. V* include both Ferrum reductum and Ferrum pulveratum.

**Incompatible** with tannin and metallic salts.

Pills of reduced iron require  $\frac{1}{8}$  to  $\frac{1}{4}$  grain of compound tragacanth powder to bind them.

**Trochisci Ferri Redacti** (*B.P.C.*) contain 1 grain.

**Vinum Ferri (B.P.C.).**

*Dose.*—1 to 4 drachms (4 to 16 ml.).

Sherry-type wine in which iron has been immersed until the liquid contains 0.125 to 0.300% w/v of Fe.

**Vinum Ferri** (*P. Jap. V*). Iron and ammonium citrate 2%, in a white wine.

**Ferri Carbonas Saccharatus** (*B.P., P. Helv. V*).

*Dose.*—10 to 30 grains (0.6 to 2 g.).

Ferrous oxycarbonate,  $x\text{FeCO}_3, y\text{Fe}(\text{OH})_2$ , partially oxidised and mixed with liquid glucose, the mixture containing not less than 50% of ferrous iron calculated as  $\text{FeCO}_3$ .

**Incompatible** with tannin-containing drugs, also with acids and acid salts.

**Uses.** For anæmia and chlorosis of young women. Ferrous salts are used in preference in anæmia as they are more readily ionised and less readily hydrolysed than ferric salts, and remain longer in the circulation than such complex salts as iron and ammonium citrate. Another point in favour of ferrous salts is that much smaller doses can be given. Large doses of iron lead to various complications, indigestion, cramps, etc.; they also change the bacterial flora and interfere with the absorption of such essential substances as minerals and vitamins.

**Mistura Ferri Composita (B.P.C.).** *Syn.* GRIFFITH'S MIXTURE.

*Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.).

Contains ferrous carbonate equivalent to about 3 gr. of ferrous sulphate per oz.

**Pilula Ferri Carbonatis (B.P.).** *Syn.* BLAUD'S PILL, PILULA FERRI, IRON PILL, MASSA FERRI CARBONATIS (U.S.P. XI).

*Dose.*—5 to 30 grains (0.3 to 2 g.). U.S.P. XI average dose 4 grains.

Each 5 grains contain about  $\frac{1}{2}$  grain of iron.

**ANÆMIA.** Massive iron therapy—up to 60 gr. of Bland's pill daily—the most effective treatment of secondary anæmia. Ferrous better than ferric salts.—*Lancet*, ii/1931, 531.

In the treatment of MICROCYTIC HYPOCHROMIC ANÆMIAS it is usually a waste of time, material, and money to give less than 45 gr. of Bland's pill or 60 gr. of iron and ammonium citrate daily in the early stages.—J. F. Wilkinson, *Practitioner*, ii/1933, 418.

In SPLENIC ANÆMIA, whether it is believed that operation is indicated or not, treatment with effective doses of iron—iron and ammonium citrate 90 gr. daily, Bland's pill 45 gr. daily, ferrous sulphate, chloride or carbonate in tablet form, 9 gr. daily—should be tried for at least 6 to 8 weeks before iron therapy is held to have failed.—L. S. P. Davidson, *Lancet*, ii/1934, 596.

In the treatment of HELMINTHIC ANÆMIA, iron in large doses (Bland's pills 3 to 4 *t.d.s.* and iron and ammonium citrate 1  $\frac{1}{2}$  to 2 grammes *t.d.s.*) combined with a well balanced diet (fats and proteins) proved most effective. Iron was found more effective in ankylostoma anæmia than in that due to intestinal bilharziasis. Liver therapy proved ineffective.—M. Salah, per *Trop. Dis. Bull.*, 1936, 33, 151.

**COMBINED DEGENERATION OF THE CORD** successfully treated by Bland's pill 150 gr. daily, in capsules. Liver treatment may be necessary in addition.—W. Sargent, *Lancet*, i/1932, 232.

**Excretion by Normal Subjects.** Two men and two women, who were in iron balance on diets containing 7 to 9 mg. per day, were each given approximately 1000 mg. of iron daily for 36 to 46 days. The iron was taken by the men in the form of iron and ammonium citrate, and by the women in the form of capsules containing 1 g. of saccharated iron carbonate. Determinations of the iron excreted were made, and after discontinuing the administration and allowing time for unabsorbed iron in the gut to be excreted, net absorptions of 1.5 to 5 g. of iron were registered. Immediately afterwards the subjects were again found to be in iron equilibrium in spite of the large amounts absorbed, and it is concluded that the body has little or no capacity for excreting iron. Changes in the hæmoglobin levels were comparatively slight. In two there was no change, in one it rose about 10% and fell very slowly, and in the fourth it rose during administration but fell immediately the iron was discontinued, in spite of the large amount absorbed.—E. M. Widdowson and R. A. McCance, *Biochem. J.*, 1937, 2029.

It is suggested that the capacity of the bowel to excrete iron has been exaggerated, particularly its capacity to regulate the amount of iron which it excretes. There are, indeed, indications that in man and certain animals the bowel excretes practically no iron. If this is the case, the amount of iron in the body must be regulated by controlled absorption.—R. A. McCance and E. M. Widdowson, *Lancet*, ii/1937, 680.

**Pilulæ Ferri Carbonatis (U.S.P. XI).** *Syn.* CHALYBEATE PILLS, FERRUGINOUS PILLS. *Average dose.*—3 pills.

Each pill contains about 1 gr. of  $\text{FeCO}_3$ .

**Pilulæ Ferri Carbonatis Compositæ (B.P.C.).** *Syn.* BLAUD'S PILL WITH ALOIN AND CASCARA.

*Dose.*—1 to 3 pills.

Contain 5 gr. of pill of iron carbonate with  $\frac{1}{10}$  gr. of aloin and  $\frac{1}{2}$  gr. of dry extract of cascara sagrada.

**Pil. Ferri et Casc. (N.I.F.).**

Pill of iron carbonate 4 gr., dry extract of cascara sagrada  $\frac{1}{2}$  gr.

[P1-81] *Pilulæ Ferri Carbonatis cum Arseno et Strychnina* (B.P.C.).  
*Syn.* BLAUD'S PILL WITH ARSENIC AND STRYCHNINE.

*Dose.*—1 or 2 pills.

Contain 5 gr. of pill of iron carbonate with  $\frac{1}{10}$  gr. of arsenic trioxide and  $\frac{1}{10}$  gr. of strychnine hydrochloride.

[P1-81] *Pilulæ Ferri Carbonatis et Arseni* (B.P.C.). *Syn.* BLAUD'S PILL WITH ARSENIC.

*Dose.*—1 pill.

Contain 5 gr. of pill of iron carbonate and  $\frac{1}{10}$  gr. of arsenic trioxide.

*Pilulæ Ferri Carbonatis Saccharati* (B.P.C.).

*Dose.*—1 to 3 pills.

Contain 3 gr. of saccharated iron carbonate per pill, equivalent to about 10 gr. of Blaud's pill.

*Tabellæ Ferri Carbonatis* (B.P.C.).

*Dose.*—1 to 6 tablets.

Contain the equivalent of 5 gr. of Blaud's pill.

*Tabellæ Ferri Carbonatis et Aloini* (B.P.C.). *Syn.* BLAUD'S TABLETS WITH ALOIN.

*Dose.*—1 to 6 tablets.

Contain the equivalent of 5 gr. of Blaud's pill and  $\frac{1}{10}$  gr. of aloin.

*Ferri Citras.* *Syn.* FERRUM CITRICUM OXYDATUM (P. *Jap.* V).

*Dose.*—5 to 15 grains (0.3 to 1 g.).

Containing ferric citrate corresponds to not less than 16% of Fe. Garnet-red soluble scales with slight ferruginous taste.

*Ferri et Ammonii Citras* (B.P. *Add. I*, U.S.P. XI, *Fr. Cx.*).

*Dose.*—20 to 40 grains (1.3 to 2.6 g.). 40 grains contains about 8 grains of iron. B.P. '32 gave max. dose 15 grains. U.S.P. XI average dose 30 grains. Contains 20.5 to 22.5% (B.P.) or 16.5 to 18.5% (U.S.P. XI) of metallic iron. Dark red scales soluble in about half their weight of water. Is also available in granules.

In debility and anæmia. Especially preferred in lingering cases of gastric catarrh after alkalis have ceased to benefit and the stomach is not ready for an acid tonic. Also with sodium salicylate in subacute rheumatism of children.

In ANÆMIA OF CHILDREN had no appreciable effect.—N. K. Gibbs, *Lancet*, ii/1929, 550.

Simple achlorhydric anæmia treated by iron and ammonium citrate. 90 gr. daily increased to 120 gr.—D. C. Hare, *Brit. med. J.*, ii/1931, 889.

CHLOROSIS in young persons well treated by iron. Chronic microcytic anæmia in mid-life treated by iron and ammonium citrate, 60 to 120 gr. daily for 4 to 5 months.—L. J. Witts, *Lancet*, i/1931, 146.

Anæmia is prevalent among nearly half the women of the poorest classes in Aberdeen, and appears to be mainly due to increased demands for iron as a result of frequent pregnancies, or of excessive blood loss during menstruation and/or parturition. The anæmia can be rapidly cured with marked improvement of general health by administration of iron salts. It is suggested that a glass of milk and a pennyworth of iron and ammonium citrate, without any other change in the diet of pregnant women of the poorest classes, would produce remarkably beneficial results to mother and infant.—L. S. P. Davidson and co-workers, *Brit. med. J.*, i/1933, 689.

The administration of iron in therapeutic doses to pregnant women converted the fall in hæmoglobin, which was then in progress, into a rise. After the administration of iron had been discontinued the hæmoglobin fell once more and at about the same rate as if iron had not been administered.—E. M. Widdowson, *Lancet*, ii/1939, 640.

*Mist. Ferri et Ammon. Cit.* (N.I.F.). Iron and ammonium citrate 20 gr., ammonium carbonate 1 gr., chloroform water to  $\frac{1}{2}$  oz.

[P1] *Mist. Ferri Cit. c. Arsen.* (N.I.F.). Iron and ammonium citrate 12  $\frac{1}{2}$  gr. arsenical solution 3 m., chloroform water to  $\frac{1}{2}$  oz.

**Vinum Ferri Citratis (B.P.C.).**

*Dose.*—1 to 4 drachms (4 to 16 ml.). Contains about 1 gr. of iron and ammonium citrate per drachm of orange wine.

**Cupriferrum** (*Squibb, New York; Savory & Moore, London*). Capsules contain 85 mg. of iron (as iron ammonium citrate) and 0.5 mg. of copper as copper gluconate. *Dose.*—6 to 12 capsules daily. Nutritional anæmia.

**Elixir Hæmotone** (*Duncan, Flockhart, Edinburgh*). Contains in each fl. dr.  $7\frac{1}{2}$  gr. of iron and ammonium citrate, with copper  $\frac{1}{10}$  gr., glycerophosphates and glucose. *Dose.*—1 to 4 teaspoonfuls three times daily.

**Iberin** (*Abbott Laboratories, London*). Capsules containing iron and ammonium citrate (B.P.) 5 gr.; vitamin B<sub>1</sub> 22 i.u.; vitamin B<sub>2</sub> 20 Sherman units; liver concentrate 4 gr. (1 part equals 20 parts of fresh liver). For secondary anæmia.

**Ferri et Ammonii Citras Viridis (B.P.C.).** *Syn.* FERRI ET AMMONII CITRATES VIRIDES (U.S.P. XI).

*Dose.*—5 to 10 grains (0.3 to 0.6 g.). Hypodermically  $\frac{1}{2}$  grain in 4% w/v solution, but for this purpose it must be neutralised with ammonia to give no red colour with either methyl red or phenol red.

U.S.P. XI average dose, by parenteral injection, 1 grain.

Green deliquescent scales prepared as for iron and ammonium citrate but using more acid and sufficient ammonia to give a green colour. Contains 14 to 16% of Fe. **Soluble** 2 in 1 of water.

**Injectio Ferri (B.P.).**

*Dose.*—15 to 30 minims (1 to 2 ml.). 30 m. contains the equivalent of about  $\frac{1}{10}$  gr. of iron.

Contains a double citrate of iron and ammonium.

Iron injections are a poor substitute for oral administration, and their use is seldom justified.

The injection tested in 10 cases. It was found to be of very low therapeutic efficiency owing to the small proportion of iron, and also painful, but this could be corrected by adding 3% of procaine hydrochloride. Double the maximum official dose can be given, but would have to be given twice daily for 6 weeks to equal the effect of large oral doses. Except in rare instances the administration of iron by the parenteral route should be avoided.—G. N. Burger and L. J. Witts, *Proc. R. Soc. Med.*, 1934, 27, 447.

Iron given by injection is quite inert; the popular and expensive ampoules of such solutions may have some effect on the mind, but they have none on the blood. When 30 gr. of iron and ammonium citrate is given thrice daily, the hæmoglobin generally increases by about 1% a day. It is unsafe to give much larger doses; 40 gr. 4 times a day for 3 weeks may cause acute iron encephalopathy.—A. F. Hurst, *Pharm. J.*, ii/1934, 675.

**[P1-81] Injectio Ferri et Arseni (B.P.C.).**

*Dose.*—8 to 15 minims (0.5 to 1 ml.) intramuscularly. Contains the same proportion of iron as Injectio Ferri together with  $\frac{1}{50}$  gr. of arsenic trioxide per 15 m.

**[P1-81] Ferarin** (*Squire, London*). Solution of green iron and ammonium citrate with arsenic for intramuscular injection.

**[P1-81] Ferri et Ammonii Citro-Arsenis (B.P.C.).** *Syn.* SOLUBLE IRON ARSENITE.

*Dose.*— $\frac{1}{10}$  to  $\frac{1}{2}$  grain (0.0015 to 0.03 g.); maximum daily dose 1 grain (0.06 g.).

A double salt of ferrous arsenite and ammonium citrate in greenish deliquescent scales containing about 14% of Fe and 1.4% of As<sub>2</sub>O<sub>3</sub>. May be administered by injection.

**Ferri et Ammonii Tartras.**

*Dose.*—5 to 15 grains (0.3 to 1 g.). In garnet-red soluble scales containing not less than 13% of Fe.

**Ferri et Mangani Citras (B.P.C.).**

*Dose.*—3 to 15 grains (0.2 to 1 g.).

In reddish scales, freely soluble in water, containing not less than 14% of Fe and not less than 7% of Mn. Useful in chlorosis, combining the action of the two elements.

**Ferri et Potassii Tartras (B.P.C.).** *Syn.* FERRUM TARTARATUM, FERRI-KALIUM TARTARICUM (*P. Jap. V*).

*Dose.*—5 to 10 grains (0.3 to 0.6 g.).

Reddish-brown scales soluble in water about 1 in 1; very sparingly soluble in alcohol 90%. Contains not less than 20% of Fe.

Menorrhagia of young females is well treated by this tartrate.

**Ferri Iodidum (B.P.C.).** *Syn.* FERROUS IODIDE.  $\text{FeI}_2 = 309.7$ .

*Dose.*—1 to 5 grains (0.06 to 0.3 g.).

Crystalline grey or brown hygroscopic masses readily soluble in water. Mostly prescribed as SYRUPUS FERRI IODIDI.

**Liquor Ferri Iodidi (B.P.C.).** *Syn.* LIQUOR PRO SYRUPO FERRI IODIDI.

*Dose.*—2 to 8 minims (0.12 to 0.5 ml.).

Contains about 53.5% *w/v* of  $\text{FeI}_2$ , and when mixed with 7 volumes of syrup forms Syrupus Ferri Iodidi.

**Syrupus Ferri Iodidi (B.P., P. Ned. V).** *Syn.* SIRUPUS FERROSI IODIDI CONCENTRATUS *I.A.*

*Dose.*— $\frac{1}{2}$  to 2 drachms (2 to 8 ml.).

Contains 5% *w/w* of  $\text{FeI}_2$ ; 2 drachms contains about  $7\frac{1}{2}$  gr. of ferrous iodide equivalent to about  $1\frac{1}{2}$  gr. of iron.

*P. Belg. IV* and *F.E. VIII* have this strength as concentrated syrups, which diluted 10 times provide dilute syrups containing 0.5% of ferrous iodide. *Fr. Cx.* and *P. Ital. V* have the same dilute syrup only.

**Incompatible** with alkalis such as sal volatile.

**ACTION OF LIGHT.** The action of light in restoring the green colour in a decomposed sample is due to conversion of the sucrose to invert sugar, the levulose of which has a complex reducing effect resulting in the re-formation of ferrous iodide. When the inversion is completed by sufficiently long exposure to light, enough levulose is present to preserve the ferrous iodide permanently. Immersion of a discoloured syrup in boiling water for an hour is as effective as exposure to sunlight in restoring the green colour.—*H. V. Army, A. Taub and W. C. Mende, per Pharm. J., ii/1936, 251.*

Addition of lactic acid does not prevent rapid development of the brown colour on exposure to light, but both citric and tartaric acids are satisfactory preservatives.—*A. Jermstad and B. Fretheim, Pharm. Zentr., 1939, 80, 545.*

**Syrupus Ferri Iodidi (U.S.P. XI).**

*Average dose.*—15 minims (1 ml.).

Approximately the same composition and strength as *B.P.* syrup, except that it contains 50% more hypophosphorous acid. *U.S.P. XI Supp. II* allows the substitution of citric acid for the hypophosphorous acid in the formula to retard discoloration.

**Ferrum Iodatam Saccharatum** (*P. Jap. V*). A preparation made by triturating lactose and reduced iron with freshly prepared solution of ferrous iodide. It contains 20% of  $\text{Fe I}_2$ .

**Syrupus Ferri Bromidi (B.P.C.).**

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Contains about  $4\frac{1}{2}$  gr. of ferrous bromide in 1 dr.

**Syrupus Ferri Bromidi cum Quinina (B.P.C.).***Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).Contains about  $\frac{1}{10}$  gr. of quinine dihydrobromide and 4 gr. of ferrous bromide in 1 dr.**[P1] Syrupus Ferri Bromidi cum Quinina et Strychnina (B.P.C.).***Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).Similar to the preceding, containing also  $\frac{1}{10}$  gr. of strychnine per dr.**[P2] Ferri Oxalas (Fr. Cx.).**  $\text{Fe}(\text{COO})_2 \cdot 2\text{H}_2\text{O} = 179.9$ . *Syn.* FERROUS OXALATE, PROTOXALATE OF IRON, FERROSUM OXALICUM (P. Belg. IV).*Dose.*—1 to 5 grains (0.06 to 0.3 g.).

Yellow crystalline powder, insoluble in water but soluble in dilute acids. Has been given in anæmia and as a nerve tonic.

**Ferri Oxidum Calcinatum.** *Syn.* FERRI SESQUIOXIDUM. Obtained by roasting precipitated oxide of iron, and usually contains about 94% of  $\text{Fe}_2\text{O}_3$ . Impure forms are Armenian bole, ochre, Venetian red, jewellers' rouge, etc.**Ferri Oxidum Præcipitatum Fuscum (B.P.C.).** *Syn.* FERRI PEROXIDUM.*Dose.*—5 to 15 grains (0.3 to 1 g.). A brown powder containing 80 to 90% of  $\text{Fe}_2\text{O}_3$ .**[P1-81-83] Emplastrum Ferri (B.P.C.).** *Syn.* EMPLASTRUM ROBORANS, STRENGTHENING PLASTER. Contains 9% of brown precipitated ferric oxide in Burgundy pitch and plaster of lead.

The name "Strengthening Plaster" is usually applied to a spread plaster which is not prepared with iron oxide, and has, therefore, an entirely different composition.

**Ferri Oxidum Præcipitatum Rubrum (B.P.C.).** *Syn.* FERRI CARB., FERRI SUBCARB.*Dose.*—5 to 15 grains (0.3 to 1 g.).

Obtained by precipitating ferrous sulphate solution with sodium carbonate and washing and drying the precipitate. A dull brownish-red powder.

**Ferrum Oxydatum Saccharatum (P. Austr., P.G. VI, P. Helv. V, P. Dan.).***Dose.*—10 to 40 grains (0.6 to 2.5 g.).

Dilute ferric chloride solution (P.G. VI—10% of Fe) 30 g. with water 150. Then add with stirring a solution of sodium carbonate 26 in water 150 (towards the end of the precipitation before each fresh addition of the alkali wait for the re-solution of the precipitate). Wash to free from chloride, collect on cloth, press slightly, mix in porcelain dish with powdered sugar 50 and so much sodium hydroxide solution (sp. gr. 1.17) as is required to dissolve on a water-bath (not more than 5 to be used), evaporate, dry, and mix with sugar q.s. to make 100.

A reddish-brown powder containing 2.8 to 3% of Fe.

**Ferri Peptonas.** A compound of iron and peptone with addition of sodium citrate to render it soluble. Usually administered as the solution in the treatment of anæmia, neurasthenia and chlorosis.**Liquor Ferri Peptonatis (B.P.C.).** *Syn.* SOLUTION OF PEPTONISED IRON.*Dose.*—1 to 4 drachms (4 to 16 ml.).

Contains 0.65% w/v of iron and 4% w/v of peptone.



**Liquor Ferri Peptonatis cum Mangano (B.P.C.).** *Syn.* SOLUTION OF PEPTONISED IRON WITH MANGANESE.

*Dose.*—1 to 4 drachms (4 to 16 ml.).

Similar to the above, but containing also  $\frac{1}{2}$  gr. of manganese chloride per drachm.

**Liquor Ferri Albuminati (P.G. VI, P. Helv. V).**

*Dose.*—1 to 4 drachms (4 to 16 ml.).

A solution containing a compound of iron and egg albumen adjusted to contain about 0.4% of Fe. *P. Ned. V* contains 0.25% of  $\text{Fe}_2\text{O}_3$ .

**Fer Ascoli (Allen & Hanburys, London).** An organic compound of iron with nuclein in tablet form. Used in treatment of anaemia.

**Ferratin (Boehringer, Mannheim; Coates & Cooper, London).** Sodium ferroalbuminate, containing 6% of iron. Tablets contain 4 grains. *Dose.*—2 tablets 3 or 4 times daily.

[P1] **Ferroarsine (Parke, Davis, London).** Solution of iron peptonate and manganese with arsenic peptonate  $\frac{1}{8}$  gr. and strychnine sulphate  $\frac{1}{128}$  gr. *Dose.*—1 to 2 fluid drachms (4 to 8 ml.) thrice daily.

**Ferri Perchloridum (B.P.C., P. Helv. V).** *Syn.* FERRI SESQUICHLORIDUM, FERRUM SESQUICHLORATUM (*P. Jap. V*).

$\text{FeCl}_3 \cdot 6\text{H}_2\text{O} = 270.3$ .

*Dose.*— $\frac{1}{2}$  to 2 grains (0.03 to 0.12 g.), or more.

Deliquescent yellow masses made by evaporating the strong solution and crystallising.

**Incompatible** with infusions, etc., containing tannin, with the alkalis, alkaline carbonates, iodides, salicylates and mucilage of acacia. With potassium iodide in presence of potassium citrate a potassium ferricitrate is formed, and hence it is compatible.

**Soluble** in water, alcohol, ether and glycerin.

**Uses.** Internally as hæmatinic, externally as astringent and styptic.

**BRONCHITIS.** The irritating dry cough may be relieved by applying a mixture of 120 gr. of ferric chloride in 2 oz. of glycerin, on cotton wool, wound round a bent probe, which is passed just to the side of the middle line as near the back of the tongue as possible into each vallecule in turn.—E. P. Poulton and F. A. Knott, *Practitioner*, 1/1936, 30.

**Garg. Ferri Perchlor. (N.I.F.).** Solution of ferric chloride 2 dr., potassium chlorate 2 dr., glycerin  $\frac{1}{2}$  oz., water to 8 oz. Dilute with 1 or 2 parts of water.

**Glycerinum Ferri Perchloridi (B.P.C.).** *Syn.* PIGMENTUM FERRI PERCHLORIDI. Solution of ferric chloride 1, glycerin 1. For use as a paint. Glycerin and chloroform water cover its metallic astringent taste.

**Gossypium Stypticum.** *Syn.* GOSSYPIUM FERRI PERCHLORIDI.

Saturate absorbent wool 85 with water 100 containing ferric chloride 15, and dry. Lintum Stypticum is made similarly.

**Liquor Ferri Dialysatus (B.P.C.).**

*Dose.*—10 to 30 minims (0.6 to 2 ml.).

A colloidal solution of ferric hydroxide containing the equivalent of 3 to 4% of Fe.

A well-tolerated, non-astringent hæmatinic. It is prescribed undiluted or mixed with 2 parts of glycerin.

Dialysed iron is useful as an antidote to arsenic—much superior to the moist peroxide; 1 ounce doses should be given repeatedly, preceded by a dose of common salt or sodium bicarbonate.

**Colliron (Evans, Sons, Lescher & Webb, Liverpool).** 10% solution of colloidal iron.

**Idozan (Coates & Cooper, London).** 5% solution of colloidal iron.

*Dose.*—1 drachm, increased to  $\frac{1}{2}$  ounce, thrice daily.

**Ovoferrin** (*A. C. Barnes, Philadelphia; Fassett & Johnson, London*). Colloidal iron tonic (1 dr. = 1 gr. of colloidal iron). *Dose*.—One tablespoonful in water or milk.

**Liquor Ferri Oxychloridi (B.P.C.)**. *Syn.* SOLUBLE PEROXIDE OF IRON.

*Dose*.—10 to 30 minims (0.6 to 2 ml.).

Contains the equivalent of about 3% *w/v* of Fe.

**Liquor Ferri Perchloridi (B.P.)**.

*Dose*.—5 to 15 minims (0.3 to 1 ml.).

Contains about 15% of FeCl<sub>3</sub>, equivalent to about 5% of Fe.

A solution of the same strength may be obtained by diluting 1 volume of Liq. Ferri Perchlor. Fort. with water to 4 volumes.

The use of iron salts applied as a lotion, compress or wet dressing should be discouraged in all vesicular, bulbous and exudative dermatoses. Two cases of permanent pigmentation following the application of 5% ferric chloride solution for the treatment of ivy poisoning.—E. F. Traub and J. S. Tennen, *J. Amer. med. Ass.*, i/1936, 1711.

**ERYSIPELAS**. Liq. Ferri Perchlor. 20 or 25 m. thrice daily acts almost as a specific. Collodion locally helps.

**TINEA CIRCINATA**. An intractable case quickly cured, after failure of iodine, salicylic acid and chrysarobin.—J. H. Boulton, *Brit. med. J.*, ii/1932, 180.

**Liquor Ferri Chloridi (U.S.P. XI)**.

*Average dose*.—1½ minims (0.1 ml.).

A solution containing 10 to 11% *w/w* of iron, and from 3 to 5% *w/w* of HCl, and therefore approximately double the strength of Liquor Ferri Perchloridi (B.P.). Liquor Ferri Perchloridi Fortis (B.P.C.) diluted with an equal volume of water would give a solution of approximately the same iron content.

**Liquor Ferri Sesquichlorati (P.G. VI)** contains 10% of Fe approx. **FERRUM SESQUICHLORATUM SOLUTUM (P. Helv. V)** is similar.

**Liquor Ferri Perchloridi Fortis (B.P.C.)**. Contains 20% Fe. Has sp. gr. about 1.43. It is four times the strength of Liquor Ferri Perchloridi.

[P1] **Mist. Arsen. Ferri et Strych. (N.I.F.)**. Solution of strychnine hydrochloride 3 m., arsenical solution 3 m., solution of ferric chloride 10 m., dilute hydrochloric acid 1 m., syrup ½ dr., water to ½ oz.

[P1] **Mist. Ferri et Strych. (N.I.F.)**. Solution of strychnine hydrochloride 3 m., solution of ferric chloride 10 m., dilute hydrochloric acid 1 m., chloroform water to ½ oz.

**Mist. Ferri Perchlor. (N.I.F.)**. Solution of ferric chloride 10 m., glycerin 20 m., water to ½ oz.

**Mistura Ferri Salina (U.C.H.)**.

Potassium citrate 22 gr., solution of ferric chloride 24 m., chloroform water to 1 oz. The styptic taste of iron is masked in this mixture, as a double decomposition occurs between the iron and the potash salt.

**Nebula Ferri Perchloridi (T.H.)**. Ferric chloride 5 gr., glycerin 15 m., water to 1 oz.

**Pigmentum Ferri Perchloridi (T.H.)** contains 1 to 2 dr. of ferric chloride per oz. of water.

**Tinctura Ferri Perchloridi (B.P.C.)**.

*Dose*.—5 to 15 minims (0.3 to 1 ml.).

A 25% dilution of strong solution of ferric chloride with diluted alcohol. Is the same strength as Liquor Ferri Perchloridi.

Owing to the fact that ferric chloride does not remove any of the acid of the gastric juice (as when reduced iron or Bland's pills are

given), this is preferred by many. Thread-worms are killed by rectal injection of 1 dr. of the tincture in 10 oz. of water.

**CUTANEOUS ERYSIPELAS.** An old effective remedy is local application of strong solution of ferric chloride, also internal use of tincture of ferric chloride.

**Tinctura Ferri Chloridi (U.S.P. XI).**

*Average dose.*—10 minims (0.6 ml.).

Solution of ferric chloride (U.S.P.) 35 ml. diluted with sufficient alcohol to produce 100 ml.

**Ferri Phosphas (B.P.C.).**

*Dose.*—5 to 10 grains (0.3 to 0.6 g.).

A slate-blue amorphous powder consisting of hydrated ferrous phosphate, ferric phosphate and some hydrated iron oxide, containing not less than 47% of ferrous salts calculated as  $\text{Fe}_2(\text{PO}_4)_2 \cdot 8\text{H}_2\text{O}$ .

**Liquor Ferri Phosphatis (B.P.C.).**

*Dose.*—4 to 8 minims (0.5 to 2 ml.).

One volume mixed with seven volumes of syrup forms Syrupus Ferri Phosphatis.

**Liquor Ferri Phosphatis Compositus (B.P.C.).**

*Dose.*—8 to 30 minims (0.5 to 2 ml.).

One volume mixed with seven volumes of syrup forms a compound syrup similar to Syrupus Ferri Phosphatis Compositus.

[P1] **Pilulæ Ferri Phosphatis cum Quinina et Strychnina (B.P.C.).** *Syn.* PILULÆ TRIUM PHOSPHATUM, EASTON'S PILLS.

*Dose.*—1 or 2 pills. Contain saccharated iron phosphate, quinine and strychnine equivalent to  $\frac{1}{2}$  dr. of Syrupus Ferri Phosphatis cum Quinina et Strychnina.

Also made twice this strength. Either may be combined with arsenic trioxide,  $\frac{1}{10}$  grain (0.001 g.).

**Syrupus Ferri Phosphatis (B.P.C.).**

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.). Contains 1 gr. of anhydrous ferrous phosphate per drachm. Is best prepared, as required, from Liquor Ferri Phosphatis.

**Syrupus Ferri Phosphatis Compositus (B.P.).**

*Syn.* CHEMICAL FOOD, PARRISH'S SYRUP, PARRISH'S FOOD.

*Dose.*— $\frac{1}{2}$  to 2 drachms (2 to 8 ml.).

Contains iron equivalent to 0.9% w/v of  $\text{Fe}_3(\text{PO}_4)_2$ , and calcium equivalent to 1.4% w/v of  $\text{Ca}_3(\text{PO}_4)_2$ . 2 dr. contains about  $\frac{1}{2}$  gr. of anhydrous ferrous phosphate equivalent to about  $\frac{1}{2}$  gr. of iron.

**Syrupus Ferri cum Mangano (Gt. Orm. H.).** (*Dose* for 1-year-old child.)

Copper sulphate  $\frac{3}{10}$  gr., manganese chloride  $\frac{1}{2}$  gr., compound syrup of ferrous phosphate to 1 dr.

[P1] **Syrupus Ferri Phosphatis cum Quinina et Strychnina (B.P.).** *Syn.* EASTON'S SYRUP, SYRUPUS TRIUM PHOSPHATUM.

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Contains iron equivalent to 1.8% w/v of  $\text{Fe}_3(\text{PO}_4)_2$ , 1.09% w/v of anhydrous quinine, and 0.0246% w/v of strychnine. 1 dr. represents 1 gr. of anhydrous ferrous phosphate,  $\frac{1}{2}$  gr. of quinine sulphate and  $\frac{1}{10}$  gr. of strychnine hydrochloride. It contains only about half the strychnine content of the B.P. 1914 syrup.

A widely-used tonic preparation.

The following formula for Easton's Syrup is suggested to replace the existing official preparation. Iron 8.6 g., phosphoric acid 35 ml., strychnine hydrochloride

0.3 g., quinine hydrochloride 13.3 ml., dilute hydrochloric acid 50 ml., syrup 660 ml., glycerin 140 ml., distilled water to 1000 ml. Dilute the phosphoric acid with 70 ml. of water, add it to the iron in a flask of suitable size, and heat on a water bath until the iron is dissolved. Add a solution of the strychnine and quinine hydrochlorides in the dilute hydrochloric acid, and filter into the syrup and glycerin previously mixed. Pass sufficient distilled water through the filter to produce the required volume.—W. T. Wing, *Quart. J. Pharm.*, 1939, 562.

**Liquores pro Syrupo Eastonii.** It is not possible to prepare solutions so that 1 part of the solution containing the iron and 1 part of that containing the alkaloids, when diluted with 6 parts of syrup, will yield an Easton's Syrup identical with that of the *B.P.* By using *Liquor Ferri Phosphatis* (*see above*) in conjunction with *Liquor Quininae et Strychninae* a very close approximation is obtained.

The Committee on Pharmacy and Pharmacognosy of the Pharmacopœia Commission (*Report* 13) have recommended the inclusion in the *B.P.* of a formula for Easton's Syrup, which provides for two concentrated liquors which can be stored and diluted with syrup at the time of dispensing. The solutions are prepared as follows:—dilute 40 ml. of phosphoric acid with 40 ml. of water and add to it 8.6 g. of iron; heat on a water-bath until the iron is dissolved, filter and pass sufficient water through the filter to produce 125 ml. Triturate strychnine hydrochloride 0.3 g., and quinine sulphate 14.8 g., with a mixture of glycerin 75 ml. and dilute hypophosphorous acid 22.5 ml.; stir until solution is complete, filter and pass sufficient water through the filter to produce 125 ml. To produce Easton's Syrup mix equal quantities of the two solutions and add three times the volume of the mixed solutions of syrup.

A purely phosphatic preparation of quinine and iron cannot be made as a single solution at any considerable concentration much higher than that of the official syrup, and there seem to be only two alternatives; either a single solution four times the strength of the official syrup, necessitating the use of ferrous chloride in place of ferrous acid phosphate, with consequent alteration of the official formula, or retention of the present formula and employing two solutions, each eight times the strength of the official syrup in their respective ingredients, for mixing in equal parts. These solutions are already formulated in the *B.P.C.*—A. J. Jones, *Quart. J. Pharm.*, 1938, 496.

[P1-81] **Liquor Quininae et Strychninae** (*B.P.C.*). A syrup differing from *Syrupus Ferri Phosphatis cum Quinina et Strychnina* (*B.P.*) only in the presence of 0.75% *v/v* of hypophosphorous acid may be made by mixing 1 oz. of this solution, 1 oz. of solution of ferrous phosphate,  $\frac{1}{2}$  oz. of glycerin, and 1 oz. of distilled water with sufficient syrup to produce 8 oz.

[P1] **Syrupus Triplex** (*B.P.C.*).

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Equal parts of Easton's Syrup, Parrish's Syrup and compound syrup of hypophosphites.

[P1] **Tabellæ Ferri Phosphatis cum Quinina et Strychnina** (*B.P.C.*). *Syn.* EASTON'S TABLETS, *TABELLÆ TRIUM PHOSPHATUM*.

*Dose.*—1 tablet. Each tablet is approximately equivalent to 1 dr. of Easton's syrup. Tablets are also made equivalent to  $\frac{1}{2}$  dr.

[P1] **Tabellæ Phosphatum et Hypophosphitum Compositæ** (B.P.C.), *syn.* TRIPLE SYRUP TABLETS, *dose*.—1 tablet, are approximately equivalent to 1 dr. of triple syrup.

**Ferrodic** (Allen & Hanburys, London). Chocolate-flavoured granules containing ferrous phosphate and glucose. 1 dr. = 10 gr. of Bland's pill or 4 dr. of Syrup. Ferri Phosph. Co. *Dose*.— $\frac{1}{2}$  to 2 teaspoonfuls thrice daily after meals.

**Ferri Phosphas Saccharatus** (B.P.C.).

*Dose*.—5 to 10 grains (0.3 to 0.6 g.).

A slate-blue powder containing hydrated ferrous phosphate with ferric phosphate and iron oxide, the ferrous iron content being not less than 60%, calculated as  $\text{Fe}_2(\text{PO}_4)_3 \cdot 8\text{H}_2\text{O} = 501.7$ .

**Ferri Pyrophosphas**,  $\text{Fe}_2(\text{P}_2\text{O}_7)_2$ , may be obtained as a white insoluble powder by interaction of ferric sulphate and sodium pyrophosphate. When Ferri Pyrophosphas is prescribed Ferri Pyrophosphas Solubilis is always required.

**Ferri Pyrophosphas Solubilis** (B.P.C.). *Syn.* FERRI PHOSPHAS SOLUBILIS, SODIO-CITRO-FERRIC PYROPHOSPHATE, FERRUM PYROPHOSPHORICUM CUM AMMONIO CITRICO (P. Helv. V).

*Dose*.—2 to 8 grains (0.12 to 0.5 g.).

Green soluble scales containing not less than 10% of Fe. P. Helv. V requires 15.5 to 17% of Fe. Darkens on exposure to light.

**Ferri Subchloridi Citratum** (B.P. Add. I). CITRATED FERROUS CHLORIDE.

*Dose*.—3 to 5 grains (0.2 to 0.3 g.).  $\text{FeCl}_2 = 126.7$ .

A buff-coloured powder with astringent, acid, metallic taste. Contains not less than 68% of ferrous iron calculated as  $\text{FeCl}_2$ , together with citric acid in an amount equal to one-tenth the proportion of ferrous chloride. It is prepared by dissolving iron in hydrochloric acid, assaying, adding the requisite amount of citric acid, evaporating and drying at  $80^\circ$ .

**Soluble** 1 in 1 of water almost entirely.

**Uses.** A convenient method of administering ferrous iron, since the aqueous solution does not readily become oxidised.

Metallic iron, colloidal ferric preparations, and the scale preparations, in which the iron is in a complex form and not readily ionised, all require to be given in large doses to produce effects. The soluble ferrous salts are the most active. The average effective dose of ferric chloride must be higher than 400 mg. of iron a day, equivalent to Liq. Ferri Perchlor. 40 minims t.d.s. Ferric chloride is less potent than ferrous chloride or ferrous sulphate, but is effective if given in sufficient amounts. It is possible that iron is not absorbed in the ferric valency, and that ferric salts are reduced to the ferrous state in the alimentary tract before absorption. If minimum effective doses of ferrous iron are prescribed, between 50 and 100% of the dose ingested may be utilised for hæmoglobin formation. Reticulocyte crises and repair of anæmia may be observed with a daily dosage as low as 22 mg. of ferrous iron by mouth. There now seems no doubt that the effective dosage of preparations of iron is directly proportional to the ease with which they yield free ferrous ions.—L. J. Wits, *Lancet*, i/1936, 1.

**Copper and Manganese as Adjuvants to Iron.** In anæmia, experiments show that while pure uncontaminated iron is ineffective, the addition of small amounts of copper, germanium, nickel, arsenic or manganese make it effective—the results being essentially the same with all the supplementary elements.

Treatment of 150 cases of anæmia with (1) copper, (2) manganese, (3) copper and manganese, (4) various combinations of copper, manganese and iron, led to the belief that the best treatment was adequate doses of iron in suitable form without any further adjuncts.—J. F. Wilkinson, *Brit. med. J.*, ii/1932, 367.

**Syr. Ferri Subchloridi** (N.I.F.). *Syn.* SYRUP OF FERROUS CHLORIDE. Reduced iron 24 gr. is placed in a loosely-covered 6 oz. bottle with dilute hydrochloric acid 1 oz., and shaken occasionally until effervescence ceases. The solution is filtered and diluted with syrup to 6 oz. Each fluid drachm contains about  $\frac{1}{2}$  gr. of iron. It should be stored away from sunlight or in brown bottles.

**Endomin Tablets** (*Reed & Carnrick, New Jersey; Coates & Cooper, London*). A proprietary containing iron 8 mg., copper 0.6 mg., manganese 0.4 mg., zinc 0.3 mg., nickel 0.03 mg., cobalt 0.03 mg. and sodium germanate 0.05 mg. *Dose*.—1 to 3 tablets thrice daily. For use in anæmia in conjunction with a palatable easily-digested diet, rich in vitamins.

**Ferosan** (*Boots, Nottingham*). Capsules each containing 3 gr. of ferrous chloride for the treatment of hypochromic anæmias. *Dose*.—1 or 2 capsules three times a day, reduced to 1 capsule daily or discontinued entirely when the blood count is restored to normal.

**Ferro-Constans** (*Richter, London*) and **Ferronyl** (*Napp, London*) are tablets of ferrous chloride 0.05 g.

**Ferri Sulphas** (*B.P., U.S.P. XI, Fr. Cx., P. Jap. V, P. Helv. V, P. Dan.*). *Syn.* FERROUS SULPHATE.  $\text{FeSO}_4 \cdot 7\text{H}_2\text{O} = 278.0$ .

*Dose*.—1 to 5 grains (0.06 to 0.3 g.).

In clear, pale, bluish-green crystals containing about  $\frac{1}{2}$  of their weight of iron.

A saturated solution with some crystals of the salt in excess keeps better than a weak solution; in the latter oxidation soon takes place.

**Soluble** 1 in  $1\frac{1}{2}$  of water and 1 in 4 of glycerin; insoluble in alcohol 90%

Is administered in the treatment of chlorosis in young females in 4-grain doses. May give results in 6 weeks.—Prof. J. A. Gunn, *Lancet*, i/1931, 146.

9 gr. of ferrous sulphate, containing 180 mg. of metallic iron, is certainly as efficacious (from the point of view of hæmoglobin increase) as 90 gr. of iron and ammonium citrate containing 1215 mg. of iron, and the same remark probably applies to similar doses of ferrous carbonate and ferrous chloride.—L. S. P. Davidson and H. W. Fullerton, *Edinb. med. J.*, 1933, 210.

**ANÆMIA IN INFANCY.** All infants of low birth weight should receive iron therapy from the second month. Iron therapy should also be used prophylactically for some weeks following infections, and in all cases where the infant appears to be pale, fatigued, and not thriving. The following prescription is both palatable and efficient: ferrous sulphate  $1\frac{1}{2}$  gr., dilute hypophosphorous acid  $\frac{1}{2}$  m., dextrose 15 gr., chloroform water to 1 dr. Three times daily at the end of a feed.—L. S. P. Davidson and H. W. Fullerton, *Edinb. med. J.*, 1933, 193.

The following mixture was found of value in the treatment of nutritional anæmia in young children: ferrous sulphate  $1\frac{1}{2}$  gr., dilute hypophosphorous acid  $\frac{1}{2}$  m., dextrose 15 gr., chloroform water to 1 dr. The mixture is prepared as follows: dissolve the dextrose in some of the chloroform water, add the dilute hypophosphorous acid, dissolve the ferrous sulphate in some chloroform water and add to the dextrose solution, and make up to volume with chloroform water. The mixture will keep stable at room temperature for over two months. The mixture was given in one or two drachm doses three times daily, the full dose being reached in 3 to 5 days, and given in this way it was always well tolerated. Treatment of 26 babies, varying in age from 6 months to 3 years produced an average daily rise in hæmoglobin content of almost 1% over the first 3 to 5 weeks of treatment.—H. M. M. Mackay and L. E. Jacob, *Lancet*, ii/1937, 570.

**Mist. Ferri Aperiens** (*N.I.F.*). *Syn.* MIST. MAG. C. FERRO. Ferrous sulphate 3 gr., magnesium sulphate 30 gr., dilute sulphuric acid 5 m., copper sulphate  $\frac{1}{2}$  gr., peppermint water to  $\frac{1}{2}$  oz.

**Mistura Ferri Aperiens** (*U.C.H.*).

Magnesium sulphate 30 gr., ferrous sulphate 2 gr., dilute sulphuric acid 2 m., peppermint water to 1 oz.

**Ferrofax** (*Crookes Laboratories, London*). Ferrous iron with vitamin B in capsules or powder. 5 minim capsules each contain ferrous iron 0.1 g., vitamin B<sub>1</sub> 16.2 units, vitamin B<sub>2</sub> 3.2 units, and traces of manganese, copper and cobalt. Treatment of nutritional anæmia. *Dose*.—One capsule three times daily.

**Neo-Ferrum** (*Crookes Laboratories, London*). A colloidal iron concentrate equivalent to 10% Fe, 9% alcohol, sugar, and flavouring. One teaspoonful = 54 gr. of Bland's pill. *Dose*.— $\frac{1}{2}$  to 1 teaspoonful 3 times daily, increasing to 2 teaspoonfuls three times daily.

**Ferri Sulphas Exsiccatus** (*B.P.*, *P. Helv. V*, *P. Dan.*, *P. Jap. V*).

*Dose*.— $\frac{1}{2}$  to 3 grains (0.03 to 0.2 g.).

Ferrous sulphate dried at 40°; it contains not less than 80% of  $\text{FeSO}_4$ .

**Pilula Ferri Sulphatis** contains 3 or 5 grains of exsiccated ferrous sulphate with syrup *q.s.* Dissolving slowly, these pills do not derange the stomach. If made with lanolin or kaolin ointment as excipient they will not crack.

[P1-81] **Pil. Ferri et Aloin.** (*N.I.F.*). Exsiccated ferrous sulphate  $1\frac{1}{2}$  gr., potassium bicarbonate 1 gr., dry extract of *nux vomica*  $\frac{1}{2}$  gr., dry extract of belladonna  $\frac{1}{2}$  gr., aloin  $\frac{1}{2}$  gr.

[P1-81] **Pilula Ferri et Arseni** (*B.P.C.*). *Syn.* PILULÆ FERRI ARSENICALES. *Dose*.—1 pill.

Contain 3 gr. of exsiccated ferrous sulphate and  $\frac{1}{20}$  gr. of arsenic trioxide.

[P1-81] **Pilulae Ferri Arsenicales cum Strychnina** are the same with  $\frac{1}{20}$  gr. of strychnine hydrochloride per pill.

**Ferræmia** (*Wilcox, Jozeau, London*). Chocolate-coated tablets containing exsiccated ferrous sulphate  $2\frac{1}{2}$  gr., dried yeast 2 gr., copper sulphate  $\frac{1}{100}$  gr., manganese hypophosphite  $\frac{1}{32}$  gr. *Dose*.—One or two tablets three times daily. Anæmia and debilitated conditions.

**Fersolate Tablets** (*Glaxo Laboratories, London*). Exsiccated ferrous sulphate 3 gr. (equivalent to 1 gr. of ferrous iron), and  $\frac{1}{100}$  gr. each of copper and manganese. *Dose*.—Three 3-grain tablets daily. In secondary anæmia.

**Hemochromin** (*G. W. Carnrick, Newark, N.J.; Brooks & Warburton, London*). Tablets containing in each exsiccated ferrous sulphate equivalent to 2 gr. of crystalline ferrous sulphate, and  $2\frac{1}{2}$  gr. of extract of liver (representing  $\frac{1}{2}$  to 1 ounce of fresh liver). For iron deficiency anæmias and general debility. *Dose*.—Two tablets three times a day.

**Liquor Ferri Persulphatis** (*B.P.C.*). A solution containing ferric sulphate equivalent to 14 to 15% of Fe.

**Liquor Ferri Tersulfatis** (*U.S.P. XI*).

A solution of ferric sulphate containing 9.5 to 10.5% *w/w* of iron. Sp. gr. about 1.43 at 25°.

**Liquor Ferri Subsulphatis.** *Syn.* MONSEL'S SOLUTION.

*Dose*.—3 to 6 minims (0.2 to 0.4 ml.).

A solution of basic ferric sulphate. When evaporated and scaled forms **Monsel's Salt or Ferric Subsulphate**,  $\text{Fe}_2\text{O}(\text{SO}_4)_2$ , *dose*.— $\frac{1}{4}$  to 2 grains (0.03 to 0.12 g.).

A spray of 20 grains to the ounce checks hæmoptysis, and internally is not irritating although astringent.

[P1-81] **Unguentum Ferri Persulphatis** (*General Hosp., Notts.*). Ferric sulphate 10 gr., almond oil  $\frac{1}{2}$  dr., conium ointment to 1 oz.

The name persulphate may be taken to mean normal ferric sulphate,  $\text{Fe}_2(\text{SO}_4)_3$ , as contained in **Liquor Ferri Tersulfatis** (*U.S.P. XI*).

## FILIX MAS

*B.P.*, *Fr. Cx.*, *P. Jap. V*, *P. Helv. V*, *P. Dan.*

*Syn.* ASPIDIUM (*U.S.P. XI*), MALE FERN.

*Dose*.—1 to 3 drachms (4 to 12 g.).

The dried rhizome and leaf-bases of *Dryopteris Filix-mas*, collected late in the autumn, divested of the roots and dead portions, and not older than one year from the date of collection.

**Dangers of filix mas.** Moderate doses almost invariably produce bilirubinemia and large doses jaundice. There is risk of chronic cirrhosis of the liver developing.

About 100 cases of serious impairment of vision have been reported following administration of filix mas, mostly in South Germany and Switzerland.

**Antidotes.** Give purgative dose of magnesium or sodium sulphate. Demulcent drinks, but avoid oils and fats. Stimulants. Keep patient warm.

**Extractum Filicis (B.P.).** *Syn.* EXTRACTUM FILICIS LIQUIDUM, LIQUID EXTRACT OF MALE FERN, OLEORESINA ASPIDII (U.S.P. XI).

**Dose.**—45 to 90 minims (3 to 6 ml.). U.S.P. XI average dose, once a day, 1 drachm (caution). Larger doses, up to 2 or 3 drachms, are sometimes given.

Prepared by ether extraction—the yield being about 9 to 10%—and adjustment with olive oil to contain 25% of filicin, the anhydride of filicic acid, stated to be inactive as a vermifuge.

**Note.**—It should be well stirred before use.

**Prescribing Note.** The taste of this preparation is very unpleasant. It is best prescribed in a capsule or, if in a draught, it may be emulsified with an equal weight of acacia or tincture of quillaia, and flavoured with an essential oil such as cinnamon.

**Uses.** For all varieties of tapeworm and *ankylostomum duodenale*. Male fern retains its supremacy as the best of all remedies for tapeworm and it is the method of choice for patients treated for the first time. (The liquid extract must be freshly prepared, as it deteriorates on keeping.) On the first evening a full dose of castor oil should be given, and for the next two days a light diet of milk, gruel, soup, etc. On the fourth morning the patient is given no food, but a full dose of magnesium sulphate to ensure purgation; two hours later from 60 to 90 m. of freshly prepared liquid extract of male fern is given in a single dose. If purgation does not follow within four or five hours, a further dose of two drachms of concentrated solution of magnesium sulphate is given, followed by a glass of hot water. Treatment by male fern in children is often ineffective, since the unpleasant flavour of the drug cannot be tolerated.

Two preliminary doses of sodium sulphate at 5 and 8 p.m. on the previous day and a water enema in the morning. Then an emulsion of extract of filix mas and infusion of senna with acacia through a duodenal tube. Dose of extract 6 ml. for adult to 2 ml. for child of 5½.—*Brit. med. J. Epit.*, ii/1929, 62.

When all other methods fail, the following is often successful: Pumpkin seed 8 g., kousso 4 g., pomegranate 4 g., made into an infusion, to which is added kamala 4 g., oleoresin of aspidium 4 g., glycerin 15 ml., mucilage of acacia 15 ml., water to 240 ml. Give in two draughts 2 hours apart, after usual preliminary treatment. Severe gastro-enteric irritation with vertigo and prostration may result, but it usually gets the worm. Or give by duodenal tube into an empty stomach the morning after a day's preparation with milk diet and a cathartic, half a dose of a senna infusion (5 in 100), and 15 minutes later 2 g. of oleoresin of aspidium and 4 g. of extract of pomegranate seed mixed with the other half of the senna infusion. Remove tube promptly. Whole worm expelled in ½ to 2 hours. No treatment of any kind for tapeworm should be repeated at a less interval than three months.—*J. Amer. med. Ass.*, ii/1928, 585



**Hautus Filicis (W.H.).** Extract of male fern 1 dr., syrup of ginger 30 m., mucilage of acacia 2 dr., peppermint water to 1 oz.

**Hautus Filicis Maris (L.H.).** Liquid extract of male fern 1 dr., syrup of ginger 1 dr., tincture of quillaia  $\frac{1}{2}$  dr., peppermint water to 1 oz.

**Mistura Filicis (Gt. Orm. H.).** (Dose for children 2 years old and upwards). Extract of male fern  $\frac{1}{2}$  dr., spirit of cinnamon 4 m., syrup 2 dr., mucilage of acacia 1 dr., chloroform water to  $\frac{1}{2}$  oz.

**Filicin.** *Syn.* FILICIC ACID.

May be extracted on the lines of the chemical assay of the liquid extract. It is a combination of various acid bodies and is soluble in ether and slightly soluble in alcohol.

An investigation on flatworms and tapeworms showed it to be an excellent helminthicide: the ingested filicin reaches the intestine, impregnates the *tænia*, passes into the blood and then into the bile and returns to the intestines, where it again acts on the parasites—this cycle being repeated many times. The drug is given in pills or capsules (in oil solution) in 12-grain doses for adults, and to children  $\frac{1}{2}$  grain for each year of age. There are no toxic effects if given in suitable doses. *Tænia* are stated to be expelled in a few hours. Combined with calomel both an anthelmintic and purgative action is obtained.—*Brit. med. J. Epit.*, i/1927, 20.

**Aspidinofilicinum Oleo Solutum (P.G. VI).** *Syn.* ASPIDINOLFILIZINÖL. A 10% solution in a neutral vegetable oil.

**Filmaron-Oil 10%** (*Boehringer, Mannheim; Coates & Cooper, London*). *Dose.*—8.5 to 20 g. *per os*; children 3 to 7 g. As an enema (following a wash-out enema) in oxyuriasis, 10 g. in an equal quantity of oil.

**Kamala (B.P.C., P. Jap. V).** *Syn.* GLANDULÆ ROTTLERÆ.

*Dose.*— $\frac{1}{2}$  to 2 drachms (2 to 8 g.).

The hairs and glands obtained from the fruits of *Mallotus philippinensis* (Euphorbiaceæ). Contains rottlerin and resins. Used as an anthelmintic against tapeworm, being administered in honey, gruel or mucilaginous suspension. Its administration should be preceded by the administration of sodium bicarbonate for 48 hours.

**Mucuna (B.P.C.).** *Syn.* COWHAGE, COWITCH.

*Dose.*—10 to 60 grains (0.6 to 4 g.). The hairs covering the fruit of *Mucuna pruriens* (Leguminosæ). Mixed with honey or treacle, it can be used as a tænicide.

## FORMALDEHYDUM (LIQUOR)

*B.P., U.S.P. XI, P. Belg. IV, Fr. Cx., P. Jap. V, P. Helv. V, F.E. VIII., P. Ital. V.*

*Syn.* FORMALIN, FORMOL.

The synonym formalin may be used only in Gt. Britain and Northern Ireland. In other countries this name is registered as a trade-mark.

[P2] "*Formaldehyde.*"

[S3] "*Formaldehyde—in substances containing less than 5%, weight in weight, of formaldehyde (H·CHO); photographic glazing or hardening solutions.*"

*Dose.*—1 minim, internally, well diluted.

An aqueous solution containing 37 to 41% *w/v* of formaldehyde, H·CHO = 30.02. Is prepared by the catalytic oxidation of

methyl alcohol. Some methyl alcohol is stated to be left in the product in order to prevent polymerisation. Sp. gr. 1.080 to 1.095. *P. Jap.* has also Aqua Formalinata 1 in 35 of the 35% preparation.

**Caution.** According to the B.P.C. a 1% solution of formalin and a 1% solution of formaldehyde both mean 1% of the pharmacopœial 40% solution. If it is desired to indicate the strength of actual formaldehyde, error is avoided by using the chemical formula, *e.g.*, 1% of  $\text{H}\cdot\text{CHO}$ .

**Antidotes.** Empty stomach by emetic. Give repeated 1 dr. doses of aromatic spirit of ammonia, or  $\frac{1}{2}$  dr. dilute solution of ammonia in  $\frac{1}{2}$  pint water. Demulcent drinks.

Poisoning of a boy, aged 7, treated by washing out the stomach and then giving a quantity of very dilute ammonia, as an attempt to produce hexamine with the formaldehyde. An uneventful recovery was made.—*Brit. med. J.*, ii/1927, 687.

**Uses.** Formaldehyde is a powerful antiseptic and disinfectant with relatively high penetrating power. Solutions or vapour produce marked irritation of all mucous membranes, and its application to the broken skin is very painful. In spite of its irritant action, however, it has been usefully employed in a wide variety of conditions.

Thus, a 1 or 2% paint has been used for diphtheria, tonsillitis and ozœna, and a 2% glycerin paint has been employed with benefit in angina follicularis. Tubercular laryngitis has been treated with a 1% solution, gradually increasing to 10%, two or three times a week, and for aphthous ulceration of the mouth a 10% suspension in collodion is said to be a useful application; both of these treatments should be preceded by a local anæsthetic.

In purulent ophthalmia and trachoma an eye-wash of 1 in 1000 to 1 in 500 is stated to give good results, though it may be found extremely painful.

Various skin diseases have also been treated by local applications of formaldehyde in different forms. For dry eczema a moist application such as 1 of formaldehyde (40%) in a starch and water jelly 99, is employed, and for weeping eczema a formaldehyde dusting powder is used. Ringworm may be cured by means of a paint, care being taken to see that the solution does not run on to the unaffected skin; one application is usually sufficient. Daily application of a 10% suspension in collodion causes warts and corns to shrivel up and fall off, and sweating of the feet may be usefully treated by application of 1 part of formaldehyde in 3 of glycerin or in 5 to 10 parts of alcohol, but this method should not be employed too frequently or over too long a period.

In addition to these local applications, formaldehyde vapour has been advocated for the treatment of phthisis (*see Muthu's Inhalants*, p. 537), but it should be borne in mind that prolonged inhalation may cause irritation of the respiratory tract.

For preserving and embalming animal tissues and museum specimens dilute about 10 times—for hardening about 25 times, but for preservative purposes a far weaker solution is sufficient.

For room disinfection and utensils 1 or 2% formalin as spray (coloured fabrics are not injured), or burn formalin disinfecting tablets, *q.v.* As a wash, up to 10% solution may be used. For furniture 1% would be suitable. Or simply *evaporate a pint of formalin per 1000 cu. ft. in an open vessel over a bunsen or spirit lamp.*

**Sterilisation of Hypodermic Needles.** The following solution is suggested for keeping hypodermic needles sterile without danger of corrosion: borax 1.5 g., solution of formaldehyde 2.5 g., liquefied phenol 0.4 g., water to 100 g.—H. Haenel, *Dtsch. med. Wschr.*, 1936, 1477.

**Fumigators** are made for room disinfection. They are arranged to be lit at the bottom of the container whilst the fumigator stands on a tray with a little water. Formaldehyde is volatilised into the room and continues to be evolved for  $\frac{1}{2}$  hour. Windows, etc., to be pasted down in the usual way where complete disinfection is required, and clothing, etc., left exposed to the vapour for 3 or 4 hours.

**Formalin Disinfecting Tablets** are prepared from paraformaldehyde (*vide infra*) for use in a vaporiser or with a night-light—20 to 25 tablets per 1000 cubic feet, the latter number ensuring thorough disinfection. Walls and furniture should first be sprayed with water.

They are also prepared of strength 0.1, 0.25 and 0.5 g.

**TERMINAL DISINFECTION** during common epidemics "a procedure erroneously founded, almost always useless, and whose practical results bear no adequate relation to the labour and cost involved." Fumigation described by Dr. Andrew Balfour as "undoubtedly a process of camouflage." "Current" disinfection, *i.e.*, sterilisation of articles soiled by patient's excreta, and prompt disposal of excreta themselves, of more value.—Prof. Chagas, *Lancet*, i/1928, 922.

**Collutorium Formaldehydi (R.D.H.).** Solution of formaldehyde 18 m., oil of peppermint 5 m., alcohol (90%) 90 m., peppermint water to 1 oz. Use half a teaspoonful to a tumblerful of water. *N.I.F.* has solution of formaldehyde 60 m., water to 8 oz. Use 1 oz. in  $\frac{1}{2}$  pint of warm water. **Garg. Formaldehyd. (N.I.F.)** is identical with the latter.

**Garg. Antiseptic. (N.I.F.).** Solution of formaldehyde 16 m., boric acid 100 gr., glycerin 80 m., water to 8 oz. To be diluted with three parts of cold water.

**Gargarisma Formaldehydi (B.P.C.).** Solution of formaldehyde 0.2% *v/v*.

[P2] **Liquor Formaldehydi Saponatus (B.P.C.)** contains 20% *w/v* of formaldehyde solution.

[P2] **Formalinsäpa, Terpiniform (P. Svec. X).**

Terpineol 5, alcohol (90%) 20, soft soap 40, formaldehyde solution 35. A pleasant, fragrant antiseptic preparation.

[P2] **Morestin's Fluid.**

**Dose.**—1 to 4 ml. injected drop by drop into the not completely evacuated sac in the treatment of hydrocele.

A mixture of formalin, glycerin and alcohol equal parts.

In the treatment of hydrocele it is generally not painful. After a few hours the scrotum swells, becomes heavy and oedematous and some liquid reforms, but this is reabsorbed. Iodine has been used in children (congenital hydrocele), but is dangerous.—St. George B. Delisle Gray, *Brit. med. J.*, i/1930, 649, 726 (correction).

[P1] **Nebula Formaldehydi.** MUTHU'S INHALANTS.

**Inhalant "A."**—Chloroform 1 dr., menthol 10 gr., pumilio pine oil 10 m., alcohol (90%) to 1 oz., with 2½% of formaldehyde (in the form of gas). **"B."**—Guaiacol 1 dr., chloroform 1 dr., menthol 15 gr., pumilio pine oil 15 m., alcohol (90%) to 1 oz. with 5% formaldehyde. **"C."**—Guaiacol 2 dr., chloroform 2 dr., menthol 15 gr., pumilio pine oil 15 m., terebene 1 dr., alcohol (90%) to 1 oz. **"D."**—Guaiacol 2 dr., iodine 1 dr., terebene 1 dr., pumilio pine oil 15 m., chloroform 2 dr., alcohol to 1 oz.

**Dose.**—About 10 drops of one of the above sprinkled on the inhaler every  $\frac{1}{2}$  to 1 hour, and used by continuous inhalation.

These inhalations are used progressively. After reaching "C," "D" is used as an alternate solution or for night use.

[P2] **Cromessol** (*Cromessol Co., Glasgow*). An antiseptic containing formalin and essential oils.

**Formadermine** (*Pharmaceutical Specialities (May & Baker) Ltd., London*). Methylene diguaiaol (a condensation product of guaiaol and formaldehyde). Supplied in the form of powder as an antiseptic and deodorant for indolent ulcers, burns, skin affections, etc. Also as a 5% toilet powder for superficial conditions.

**Formosyl** (*Martindale, London*). A liquid formaldehyde potash soap. It is highly antiseptic, relatively non-poisonous, and miscible with water and alcohol in all proportions. Action of soap with the antiseptic power of formalin. A 2% solution is sufficient for general purposes and is better freshly prepared. For hand disinfection 1 to 2% is suitable. The stock bottles should be kept well corked. Available also as flavoured mouth-wash, gargle, tooth paste, etc.

**Paraformaldehydum** (*B.P.C.*). *Syn.* PARAFORM, PARAFORMIC ALDEHYDE, TRI-OXY-METHYLENE (*Fr. Cx.*), FORMALDEHYDUM POLYMERISATUM (*P. Belg. IV, U.S.P. XI, F.E. VIII*). ( $\text{H}\cdot\text{CHO}$ )<sub>3</sub> = 90.05.

A white amorphous powder or friable mass, odourless at ordinary temperatures, but having a pungent odour when warmed, owing to evolution of formaldehyde. Is prepared by evaporating aqueous formaldehyde solution; the polymer ( $\text{H}\cdot\text{CHO}$ )<sub>3</sub> throws out, and on drying changes to paraformaldehyde.

Catheters may be maintained aseptic by wrapping in lint impregnated with 20% of paraformaldehyde. A 25% solution in collodion has been employed as an application to warts.

**Paraform Collodion**, 25% strength, applied 3 times a day to warts is efficacious.

**DENTAL USE.** Paraformaldehyde, for the induction of painless dentine drilling, is mixed with Harvard Cement in the proportion of 1 to 20, and then made into a fairly firm mass with the fluid. If left in the cavity from 1 to 3 months, the cavity may be shaped without any pain to the patient. In addition, the slow emanation of formaldehyde gas over a lengthy period most probably arrests the process of decay. The cement should not be placed closer than half way to the nearest point of the pulp.

**Pasta Formaldehydi** (*R.D.H.*). Powder thymol 1 dr., and add paraform 3 gr., glycerin 10 m., zinc oxide 2 dr.

**Tabellæ Formaldehydi** (*B.P.C.*). *Syn.* FORMALDEHYDE AND MENTHOL TABLETS, FORMAMINT TABLETS.

**Note.** The general use of the names "Formalin" and "Formamint" for tablets of formaldehyde is limited to Gt. Britain and Northern Ireland.

**Dose.**—1 or 2 tablets. Contain about  $\frac{1}{2}$  gr. of paraformaldehyde and  $\frac{1}{8}$  gr. of menthol.

**Formaldigen** (*Hewlett, London*). Brand of formaldehyde lozenges.

**Formitrol Pastilles** (*Wander, London*). Brand of formaldehyde pastilles.

**Acetaldehydum.** *Syn.* ALDEHYDUM ABSOLUTUM.  $\text{CH}_3\cdot\text{CHO}$  = 44.03. A colourless mobile liquid, irritating when inhaled. Sp. gr. 0.80; b.p. 21°. Becomes acid on keeping exposed to air—oxidation to acetic acid. Polymerises with rapidity in presence of sulphuric acid at atmospheric temperature into paraldehyde (*vide infra*), but if temperature be below 0° crystalline metaldehyde is formed.

**Acetaldehydum Dilutum.** Contains 15% v/v in alcohol, is neutral to test paper, and has an ethereal suffocating odour, producing spasm of the glottis when respired. Diluted 1 in 1000 with water at 140°F. has been used as inhalation in catarrh and ozæna.

**Paraldehydeum** (*B.P.*, *U.S.P. XI*, *Fr. Cx.*, *P. Ital. V*, *F.E. VIII*, *P. Helv. V*). ( $C_2H_4O$ )<sub>3</sub> = 132.1.

*Dose*.—30 to 120 minims (2 to 8 ml.), or more, in diluted syrup or almond mixture, repeated if needed in  $\frac{1}{2}$  an hour. *U.S.P. XI* average dose 30 minims.

A colourless liquid, crystallising below 11°; sp. gr. 0.998. May be obtained by treating aldehyde with sulphuric acid.

It has been stated (*R. Hutchison, Brit. med. J.*, i/1930, 718) that paraldehyde may be oxidised by atmospheric oxygen, forming glacial acetic acid, but this does not occur under normal conditions of storage.

**Decomposition on Storage.** Samples which are free from preservative deteriorate markedly on storage even when protected from light, particularly if stored in incompletely filled containers. The main changes taking place are the formation of peroxidised compounds and an increase in acidity. While some samples show an increased aldehyde content on standing, this is unusual; there is generally a decrease due to polymerisation. Experiments on a freshly distilled sample showed that an amber-glass bottle was better than one of white glass, possibly due to differences in the composition of the glass, since no difference was noted in 2 samples, both in white glass bottles, one stored in the dark and one in the light. It is recommended that the Pharmacopœia should sanction the addition of a preservative.—*J. S. Toal, Quart. J. Pharm.*, 1937, 439.

**Soluble** 1 in 10 of water, and miscible with alcohol, ether, chloroform and oils.

If prescribed in greater proportion than will form a solution, it may be suspended with *Pulv. Tragacanth. Co.*

**Antidotes.** Empty stomach by emetic or stomach tube. Keep patient warm and awake, but do not walk him about. Ammonia inhalations. Strong coffee, with 5% dextrose, by rectum. Strychnine,  $\frac{1}{4}$  gr., hypodermically. Oxygen, or oxygen with 7% carbon dioxide, and artificial respiration if necessary.

Recovery after taking 2 oz. of paraldehyde. Stomach washed out with weak sodium bicarbonate solution; strychnine, Coramine and pituitrin administered; 1 pint of saline given intravenously; oxygen with carbon dioxide inhalations; 3 oz. of black coffee by rectum.—*W. More, Brit. med. J.*, i/1934, 428.

Paraldehyde 9 dr.—the customary drachm per stone weight—in 5 oz. of olive oil *per rectum* for dental operation. Error in copying by a third party, stating 9 oz., caused death.—*Lancet*, i/1929, 247.

**PARALDEHYDE HABIT.** 18 cases observed in 8 years. If a nightly dose of 2 dr. is continued for several weeks there is loss of appetite, gastro-intestinal irritation and flatulence; the patient becomes irritable, morose and suspicious, and may be mentally confused and agitated, with muscular weakness and tremor of hands. Tolerance is established and increased dose demanded (max. single dose of  $\frac{1}{2}$  ounce often known to be exceeded). The final picture is one of mental and physical deterioration. Paraldehydism always superimposed on other forms of addiction, most commonly alcoholism. Alcohol and paraldehyde tend to reinforce one another in action.—*A. E. Carver, per Lancet*, i/1934, 408.

**Contraindications.** Paraldehyde is contraindicated in the presence of gastric or intestinal disorder owing to its irritant effect on the mucous membrane, and in bronchitis and pulmonary affections since its pungent and disagreeable odour is likely to excite cough. It may sometimes give rise to a rash and small doses may cause a condition of excitement. Administration over prolonged periods should be avoided owing to the possibility of addiction.

**Uses.** Paraldehyde has a hypnotic action similar to that of chloral hydrate, but has a less depressant action on the heart. In moderate doses it produces a sleep resembling natural sleep and unaccompanied by any marked change in circulation, respiration or sensibility. In large doses it produces a comatose condition.

It is a valuable hypnotic for the relief of insomnia without pain, its effects being exerted within 15 to 30 minutes and lasting for two to three hours. It is most frequently used in mental conditions, e.g., for soothing maniacal patients and for inducing sleep in melancholia, and it is one of the best hypnotics for use in delirium tremens.

In spasmodic asthma it relieves the spasm by dilating the bronchioles, and it has been employed in tetanus by intravenous injection, 5 ml. being injected once or twice daily, increasing to 15 ml., and alternated with saline injections.

Paraldehyde *per rectum* is regarded as the safest of the basal hypnotics, especially for children, the dose being calculated on the basis of 1 dr. per stone bodyweight administered in 10% dilution in normal saline and given thirty minutes before operation; it is more likely to give rise to excitement, however, than other basal hypnotics. It is also employed by rectal injection, in association with other drugs, for the production of analgesia in childbirth.

In the treatment of the *status epilepticus*, paraldehyde by rectum in a dose of 6 dr., the dose to be repeated if necessary, is a valuable remedy.—E. Bramwell, *Practitioner*, ii/1933, 333.

**RECTAL ANÆSTHESIA.** Rectal paraldehyde as preliminary to tonsillectomy in children is of value. 1 dr. in 1½ oz. of saline, neither warmed nor cooled, per stone weight, an hour before operation.—M. Sourasky, *Brit. med. J.*, ii/1930, 993.

Valuable as a basal hypnotic, *per rectum*, 1 dr. per stone, given slowly 1½ hours before operation in 10 times its quantity of normal saline. Atropine as usual, and morphine to adults. Specially useful for children.—I. W. Magill, *Lancet*, i/1931, 353. Easy to work with on the upper air passages.—C. H. Thomas, *ibid.*, 354.

The evening before operation give an enema or a sedative. The following morning, 1½ hours before operation, give 1½ gr. of atropine hypodermically and immediately afterwards 8 dr. of paraldehyde (less if patient under 8 stone) in 12 oz. of saline, freshly mixed and thoroughly shaken. The paraldehyde must be fresh. The patient remains comfortable for 24 hours following operation, and distressing recollections are absent.—J. Duke Stewart, *Brit. med. J.*, ii/1932, 1139.

**LABOUR.** While there can be no doubt that in some selected cases, the use of paraldehyde, given in oil *per rectum* during the first stage of labour, may be a valuable means of relieving pain, the general opinion of those who have used it as a routine method in this investigation is that it is unsuitable for general use by midwives.—Report of an Investigation by the College of Obstetricians and Gynecologists at the request of the National Birthday Trust Fund, *per Lancet*, i/1936, 283.

Experience in 611 cases shows that the combination of paraldehyde and benzyl alcohol closely approaches the ideal for obtaining analgesia and amnesia during labour with safety for mother and child; it is accompanied with fewer undesirable reactions than any other existing method for relieving labour pains. Of particular importance in the technique is the thorough cleansing of the lower part of the bowel and rectum with a soapsuds enema, followed by irrigation with physiologic solution of sodium chloride until the return is absolutely clear. The dose of paraldehyde is 1·2 ml. to each 10 pounds of the weight of the woman at the beginning of labour. The dose of benzyl alcohol is always 1·5 ml. The mixture of paraldehyde and benzyl alcohol is instilled by gravity into the rectum by means of a funnel and a large catheter, which is inserted to a distance of

about 4 inches. As the solution disappears it is followed by not more than 30 ml. of physiologic solution of sodium chloride to wash out the catheter and distribute the drug. The mixture is given as soon as the patient complains of pain. The dose may be repeated if necessary after 1½ hours. As labour progresses the effect of each successive injection is more lasting, the intervals between repetitions becoming three, four or five hours. If the patient is awake half an hour after the initial instillation ½ gr. morphine is given subcutaneously. When several doses of the mixture are given the rectum should be irrigated with physiologic sodium chloride solution before each alternate instillation. A glass of orange juice or water should be given before each instillation and catheterisation is performed every 8 hours to relieve bladder distension. It is important that the rectal injection is repeated when the patient begins to awaken and not after she has become restless. Complete relief from the memory of pain was accomplished in 89.7% of cases, partial relief in 2.6% and no relief in 7.7%. Patients sleep for 6 to 12 hours after labour and awaken refreshed.—H. F. Kane and G. B. Roth, *J. Amer. med. Ass.*, ii/1936, 1710.

See also *Gwathmey's Method*, p. 150.

### Elixir Paraldehydi.

*Dose.*—1 to 3 drachms (4 to 12 ml.).

Paraldehyde 240, glycerin 240, alcohol (90%) 480, oil of cinnamon 4, oil of bitter orange 8, saccharin 1.

### Enema Paraldehydi (B.P.C.).

*Dose.*—1 drachm (4 ml.) per stone body weight with 5% w/v dextrose in normal saline.

### Mistura Paraldehydi.

Paraldehyde 2 dr., essential oil of almond (s.A.P.) 3 m., syrup 1 oz., liquid extract of liquorice 2 dr., water to 4 oz. This covers the nauseous taste to some extent and forms four doses of ½ drachm or two doses of 1 drachm.

### Mistura Paraldehydi et Potassii Iodidi.

*Dose.*—1 drachm (4 ml.).

Paraldehyde 1.25, potassium iodide 0.92, liquid extract of liquorice 6.25, water to 100.

In broncho-pneumonia and capillary bronchitis of infants it is valuable. The constituents of the mixture are incompatible, free iodine being formed but not sufficient to harm. In severe cases the secretions dry up remarkably.

**Metaldehyde.** A polymer of acetaldehyde occurring as a white crystalline solid, burning readily and subliming at 100°.

**Meta (Napp, London).** Compressed metaldehyde for use as a solid fuel, burning with a non-luminous carbon-free flame.

Poisoning in a boy of 16 through taking 5 g. of metaldehyde. Treatment consisted in giving large doses of alkalis and controlling the convulsions with chloral hydrate and potassium bromide.—*Lancet*, ii/1927, 670.

Two cases of poisoning in children after eating the tablets in mistake for sweets—acute poisoning of the central nervous system. Treatment: gastric lavage and purge.—*Brit. med. J.*, i/1929, 120.

Death of a young woman student after eating nearly an ounce.—*Lancet*, ii/1933, 194.

Poisoning in a child of 20 months—recovery.—A. French, *Brit. med. J.*, ii/1935, 974.

Fatal case of poisoning in a child of 2½ after swallowing one tablet. The public should be warned of Meta's dangerous qualities, and the State should introduce measures for a safer distribution.—D. R. Lewis *et al.*, *Brit. med. J.*, i/1939, 1283.

**Meta Poisoning Treatment.** (1) Immediate wash-outs of stomach with large quantities of sodium bicarbonate solution; repeat frequently and perform slowly for first time, (2) high colon wash-outs of bowels with alkaline solutions, (3) purgatives after washing-out—Glauber's salts or castor oil, (4) large quantities of charcoal (preferably wood), (5) caffeine, and, if necessary, strophanthin intravenously, (6) no narcotics if possible—sodium barbitone if cramps intensive, (7) calcium gluconate intravenously and 30 to 40% dextrose repeatedly intravenously.

## GELATINUM

*B.P., U.S.P. XI, Fr. Cx., P. Jap. V, P. Dan.*

Nearly colourless transparent sheets or shreds made by extracting animal tissues, bones, etc., with boiling water.

**Skin Gelatin** is the best. It is more pliable, possesses more "fibre," and is suitable for gelatin capsule-making. Bone gelatins made from osseine (acidulated bone) are brittle and hence unsuited. *U.S.P. XI* requires gelatin for capsule-making to contain not more than 0.15% of  $\text{SO}_2$ .

*Dose.*—*Ad libitum per os*, and injected.

*Uses.* Gelatin taken *per os* is easy of digestion, the cleavage products being largely absorbed, and it has been widely employed as a nutrient. It lacks, however, two important amino-acids, tryptophane and tyrosine. It is first converted by pepsin into proteoses and peptones. Trypsin of the pancreatic juice then splits these into amino-acids. Hypodermically the 1 to 2% solution has been used to check bleeding from the lungs and kidneys and to relieve aortic aneurism. 100 ml. or more of 2% solution may be injected into the gluteal region. These injections may be followed by pain, fever, local swellings and nettle rash. Other hæmostatics may be combined with it. It has been given orally to arrest hæmorrhage of the stomach in ulcer and cancer, and of the intestines in typhoid and dysentery. Oozing hæmorrhage from mucous surfaces due to snake bite is also well treated by large quantities given orally. Solutions of gelatin for injection must be sterilised with great care, since tetanus spores are liable to be present.

On theoretical grounds its use was suggested as a source of amino-acetic acid (glycine, *q.v.*) in the treatment of myasthenia gravis, but in clinical trial it was found to be unsatisfactory.

**Gelatina Soluta Sterilisata** (*P. Helv. V*) is approx. 9% in normal saline. The warm solution is mixed with the white of an egg, heated in an autoclave until a temperature of  $120^\circ$  is reached (should not occupy more than 30 minutes), then allowed to cool to normal pressure and filtered. It is distributed into sterile tubes which are sealed and steamed for half an hour on three consecutive days. The tubes are then incubated for a week at  $37^\circ$ , and any contaminated are rejected.

**Liquor Gelatinæ Sterilisatus** (*P. Jap. V*) is similar, but strength of sodium chloride is 0.5%.

**Soluté Injectable de Gélatine** (*Fr. Cx.*).

Gelatin 10 g., sodium chloride 8 g., distilled water to 1000 ml. Neutralise to bromo-thymol blue accurately by adding drop by drop N/10 sodium hydroxide. Sterilise for 15 minutes at  $115^\circ$  in an autoclave.

**Formalised Gelatin.** This has been used with success as a substitute for collodions. Gelatin solution 10% in water is stored in wide-mouth test-tubes holding 3 oz. each. The tubes are plugged with cotton wool and sterilised, at  $100^\circ$  for 15 minutes, on three successive days. When required for use, melt in a water-bath and add 1 dr. of formalin solution diluted 10 times, *i.e.*, 4% strength of formaldehyde approx.—the final product will then contain a little over 1% of formaldehyde, or fully 2½% of commercial formalin solution.

The wound is dressed with a thick roll or pad of sterilised gauze, with a piece of stiff gauze above extending beyond the wound. The formalised gelatin is applied with a swab on the top of the stiff gauze beyond the limit of the wound—this holds the dressing in place without bandage.



**Capsulæ.**

Capsules are made with a gelatin base and varying quantities of glycerin according to the degree of flexibility required. They are used for a variety of medicaments and are particularly suitable for nauseating oils. Soft gelatin capsules may be used for both liquid and solid medicaments, but it is unusual to put liquids into the hard type of gelatin capsule. Soft capsules are obtainable in various sizes having capacities of 3, 5, 10, 15, 20, 30, 60 and 90 minims. Hard capsules are obtainable in sizes which will hold 3, 4, 5, 6, 8, 10, 15, 25 gr. of sodium bicarbonate. A special form of soft gelatin capsule, made and filled by machinery, is known as a "perle." Soft capsules are to be preferred to the hard variety because they are more easily swallowed. Aqueous liquids tend to soften the capsule and should not, therefore, be prescribed in such containers. If it is necessary to include them, they should either be evaporated to low bulk and mixed with almond oil or they should be emulsified in almond oil using a little wool fat or white wax as emulgent. Liquids such as creosote and various volatile oils may cause discomfort in the stomach if dispensed undiluted in capsules. They should be mixed with four times their volume of almond oil and then capsuled.

**Glutoid (Enteric) Capsules.**

These may be hard or soft gelatin capsules and are intended to pass unchanged through the stomach and dissolve in the intestines. For this purpose they should be filled and sealed in the usual manner, then immersed for 5 minutes in solution of formaldehyde diluted with three times its volume of water and afterwards dried. Variable results may be obtained owing to variation in the composition of the capsule base. The action of the formaldehyde on the gelatin varies with the time of immersion and the amount of gelatin present. Moreover, the hardening effect of formalising increases on keeping and they should, therefore, be freshly prepared. The finished capsules may be tested in the following manner: they should not dissolve in an aqueous solution of glycerin of pepsin and hydrochloric acid when immersed for two hours at 37°, but should dissolve in an alkaline pancreatin solution at the same temperature. Glutoid capsules are useful for (a) drugs which may be inactivated in the stomach such as pancreatin or ox bile; (b) drugs which are more efficacious if they reach the intestines in a concentrated form, such as anthelmintics, intestinal disinfectants, and drugs like emetine and emetine bismuth iodide.

**Slipules (Martindale, London), and Pulvules (Lilly, London)** are hard gelatin capsules of the "slipover" variety.

**Lamellæ.**

Ophthalmic lamellæ or discs are prepared with gelatin, glycerin and water. The discs are  $\frac{1}{8}$  inch (3.175 mm.) in diameter. Directions for making them are given in the B.P.

**Pastilli.**

Pastilles consist of a basis of gelatin with varying quantities of glycerin. The medicament is dissolved or suspended in the melted mass, which is then moulded in oil-lubricated moulds.

The B.P.C. recommends **Glycogelatin** as a basis for pastilles. This has gelatin 20, glycerin 40, sucrose 5, citric acid 2, sodium benzoate 0.2, oil of lemon 0.1, solution of bordeaux B 1, triple orange-flower water 6.25. The gelatin is softened in water, the glycerin added and the mass evaporated down to 85. The other ingredients are then incorporated. This basis gives a soft pastille which quickly dissolves in the mouth. As the medicament is intended to have a prolonged local action, the basis should be firm enough to ensure that the pastilles dissolve very slowly. The usual commercial medicated pastille contains a higher proportion of gelatin and dissolves slowly in the mouth. They are moulded in dry starch moulds and then thoroughly dried in trays for several weeks.

**Glyco-gelatin (T.H.).** Gelatin 1 oz., glycerin 2½ oz. (by weight), orange-flower water 2½ oz.; soak the gelatin in the water, then heat until dissolved, add the glycerin and, when nearly cold, carmine solution q.s. Is a softer basis than that of the B.P.C.

**Gelatinum Glycerinatum (U.S.P. XI).** Soak gelatin 1, for 1 hour, in boiled and cooled water to cover it. Drain and add glycerin 1 (by weight), heat to dissolve, strain and evaporate to 2.

**Ichthyocolla (B.P.C., P. Belg. IV, F.E. VIII, P. Ital. V).** *Syn.* ISINGLASS, COLLE DE POISSON (*Fr. Cx.*).

The swimming bladder of certain species of the sturgeon and hake, dried and sliced into thin pieces. About 3 drachms to the pint of warm water forms a jelly. Is used for refining wine. Isinglass plasters on muslin or on silk (court plaster) are prepared with a 1 in 6 or 1 in 8 solution.

**Sinclair's Glue.** For applying extension in fractures instead of plaster. Melt on water-bath when required and apply with the hand, using a bandage if necessary.

Very good glue or gelatin 50, water 100, glycerin 4 or 6, thymol or menthol 0.15%. The smaller amount of glycerin is for summer or tropical use and the larger amount for winter. The blistering occasionally reported is due to the excessive pull exerted by the gauze. If patient complains of a tickling or burning sensation, the dressing must be removed, or in any case every 10 to 14 days.

When extra traction is needed, or for very tender skins, the following formula is occasionally used:—Isinglass 50, gelatin 50, water 200, tannic acid 12, glycerin 8 or more, thymol or menthol 0.15%.

Previous formulæ containing calcium chloride are no longer used.—W. A. Knight, *Pharm. J.*, i/1935, 7.

**Pectin.** A complex carbohydrate contained in many fruits and vegetables, and particularly in apples, beets, and the peel from citrus fruits. It has a sweetish glutinous taste, and reduces Fehling's solution. When boiled with sugar in acid media it forms a jelly, and is extensively used in the manufacture of jams and jellies for setting purposes.

Powdered pectin is obtainable commercially in a highly refined form and standardised to a definite "setting power." The standard strength usually employed is "100-Grade," 1 lb. of which will set 100 lb. of sugar in solution to a jelly of standard strength and firmness containing 65% of sugar. For medicinal and toilet purposes a pectin of about "190-Grade" is employed (pure pectin is approximately "200-Grade").

Pectin-sugar-acid gels can be obtained with 0.125% of pectin, but jams usually contain 0.5 to 1%. For 1% pectin the lower limit for sugar content is 50%, and the higher 75%. Less than 66% sugar grows moulds and yeasts. Gooseberry juice, apple and lemon are used commercially as additions where the fruit is not rich, e.g., strawberry, cherry, raspberry, blackberry, rhubarb.—S. Back, *Pharm. J.*, ii/1931, 44.

A powder consisting of pectin 10 g., tragacanth 12 g., acacia 16 g., gelatin 7.8 g. is a good emulsifying agent. 18 g. of the powder triturated with 100 g. of water, allowed to stand for 30 minutes and then 400 g. of boiling water gradually added will emulsify 400 g. of cod-liver oil, added in 5 separate portions with vigorous shaking.—W. Brandrup, per *Chem. & Drugg.*, ii/1934, 778.

Formulæ for preparing non-greasy ointments with pectin as base.—A. Mosig, *Pharm. Zentralh.*, 1937, 78, 1.

**Uses.** Apart from its commercial uses pectin has been employed for various therapeutic purposes. Internally, it may be used in the treatment of diarrhoea and probably forms the basis of the "raw apple" treatment of infantile enteritis. Its mode of action is uncertain, but it is thought to act by the adsorption of toxins. It is also stated to reduce the clotting-time of the blood, and has

been employed as a hæmostatic for external and internal hæmorrhage, being given either orally, or by subcutaneous or intramuscular injection, or in the form of a compress.

**DIARRHŒA.** The following preparation was designed to provide a product which could be administered to infants suffering from diarrhœa; dextrin and maltose 175 g., acid-free pectin 6 g., agar-agar finely ground 8 g. The substances are mixed dry, water or milk boiled with the mixed powders for 5 minutes and the product poured into 8 custard cups to form a day's feeding on a three-hour schedule.—M. Winters and C. A. Tompkins, *Amer. J. Dis. Child.*, 1936, 52, 259.

The following preparation was successfully employed in the treatment of diarrhœa in infants and the new-born: pectin 6.3%, agar 4.3%, dextrimaltose 89.4%. For nurslings 1 cup of the powder is cooked for 10 minutes in a double boiler with 24 ounces of milk, and the desired amount poured into feeding bottles while still hot, being rewarmed and shaken when required for use. The usual feeding schedule is continued. For children from 6 months to 2 years of age 8 ounces of the powder is cooked for 10 minutes with 16 ounces of milk. In a series of 23 cases of enteritis in the new-born complete recovery occurred in all.—P. J. Howard and C. A. Tompkins, *J. Amer. med. Ass.*, i/1940, 2355.

**HÆMOSTATIC.** Of 96 cases mostly tonsillectomy treated with a pectin preparation, 95 clearly demonstrated its hæmostatic properties.—T. Langner, *Ned. Tijdschr. Geneeskunde*, 1937, 81, 188.

A valuable hæmostatic in tonsillectomy. It is applied on a small swab, which is placed on the tonsil cavity and allowed to remain there for 3 or 4 minutes.—D. Guthrie, *Lancet*, ii/1938, 751.

**Aplona** (Coates & Cooper, London). Preparation of apple pectin for the treatment of diarrhœa.

**Arhemapectyl** (Bengue, London). A colloidal isotonic solution of pectin for use in hæmorrhage. Is non-toxic by ingestion up to 80 ml. 1% solution, and has no contraindications. Supplied in ampoules.

**Nipectin** (Lilly, London). A preparation of pectin with 0.15% of nickel for the treatment of diarrhœa and enteritis. The presence of the nickel is stated to increase the solubility and bactericidal activity.

**Apple Powder.** The feeding of apple pulp (the "raw apple" treatment) was found to be an effective therapeutic measure in the treatment of infantile diarrhœa. The use of the pulp was later replaced by apple powder, which is more conveniently administered. The powder is prepared from the cored and peeled apple, and although a proportion of the vitamin A and C content is destroyed in the preparation of the powder, it is stated that the pectin content is actually increased. It has been mainly employed in the treatment of diarrhœa in infants, but is also claimed to have a definite field of usefulness in the treatment of gastrointestinal diseases in the adult. Since it is probable, however, that the value of apple pulp or powder lies mainly in the pectin content, the use of pectin itself would seem to be a more rational procedure and is, in fact, becoming increasingly preferred.

**DIARRHŒA, INFANTILE.** Raw apple treatment, consisting of giving 1 to 4 tablespoonfuls of apple pulp every hour or two for 48 hours and nothing else to eat or drink, successful in 88% of cases.—T. L. Birnberg, per *Brit. med. J.*, i/1933, 624.

Fresh prepared apple powder better, 30 to 50 g. daily, soaked in warm water; diarrhœa completely arrested within 18 hours. Not suitable for children under 9 months.—P. Freud, *Brit. med. J. Epit.*, ii/1934, 67.

130 cases of acute enteritis in children from 4 months old treated with the raw apple diet with only 1 death.—J. Giblin and M. Lischner, *Arch. Pediat.*, 1935, 355.

23 cases of diarrhœa in patients varying from a few days to 8 years old treated with uniformly good results by raw apple treatment.—M. F. Borowsky, *Amer. J. Dis. Child.*, 1936, 51, 1487.

The advantages of the powder over the apple pulp are: (1) the powder represents a product of high and uniform potency; (2) the æsthetic difficulties of taste and colour are overcome; (3) co-operation of parents is more easily obtained; (4) the bulk of the apple pulp makes dosage difficult; (5) the pulverised cellulose threads of the powder make a smoother stool; (6) the powder can be added easily to milk formulæ and will produce no curdling; (7) it represents a product of uniform price available at all times of the year; (8) it keeps well, is light and compact; (9) it is not rejected when given to children who are vomiting. In children it may be given in the form of 10% apple-powder water.—I. A. Manville *et al.*, *Canad. med. Ass. J.*, i/1937, 252.

**Ivax** (Boots, Nottingham). An extract of apples, containing Ext. Malorum (10 in 1) 46.5, sucrose 28.0, water to 100.0, for the treatment of diarrhoea in infants and children, colitis, dysentery, etc. Each fluid ounce represents 4 oz. of fresh apples. *Dose*.—Infants up to 1 year of age, 2 to 3 fl. oz. daily. For older children,  $\frac{1}{2}$  to 1 fl. oz. every two hours.

## GELSEMIUM

B.P.C.

*Syn.* GELSEMI RADIX.

[P1] "*Alkaloids, the following; their salts, simple or complex:—Gelsemium, alkaloids of.*"

[S1] "*Alkaloids, the following; their salts, simple or complex:—Gelsemium, alkaloids of, except substances containing less than 0.1% of the alkaloids of gelsemium.*"

[S6] "*Alkaloids—Gelsemium, alkaloids of—specify proportion as the proportion of any one alkaloid of gelsemium that the preparation would be calculated to contain on the assumption that all the alkaloids of gelsemium in the preparation were that alkaloid.*"

*Dose*.— $\frac{1}{2}$  to 1 grain (0.015 to 0.06 g.).

The dried rhizome and roots of "yellow jasmine," *Gelsemium sempervirens* (Loganiaceæ), imported from the United States. Must be distinguished from the yellow jasmine cultivated here, which is a species of *Jasminum*. The drug contains the alkaloid gelsemine and an amorphous mixture of alkaloids called gelseminine. The latter has the greater physiological activity.

**Antidotes.** Empty stomach by emetic or by stomach tube, using dilute solution of tannic acid. Keep patient warm; give brandy,  $\frac{1}{2}$  oz., or aromatic spirit of ammonia,  $\frac{1}{2}$  dr., in water. Artificial respiration and oxygen with 7% carbon dioxide inhalations if necessary.

Accidental death from an overdose in the case of a woman suffering from neurasthenia.—*Pharm. J.*, i/1927, 558.

Even small doses sometimes cause delayed symptoms of toxicity. The warning signs are ptosis, double vision, dilated pupils, weakness and depression. A drachm of fluid extract has caused death and a dose of 30 minims is dangerous.—Sollman, 5th Edn., 1936.

**Uses.** Febrifuge, antispasmodic and analgesic. In acute and rheumatic neuralgia, toothache, uterine and ovarian pain and chorea. It is a powerful paralysant and respiratory poison. Large doses contract the pupil and cause giddiness and diplopia.

**[P1-81] Extractum Gelsemii (B.P.C.).**

*Dose.*— $\frac{1}{2}$  to 2 grains (0.03 to 0.12 g.). A soft extract.

**[P1-81] Extractum Gelsemii Liquidum.** By percolation with a mixture of alcohol 4 and water 1. Strength 1 = 1. *Average dose.*— $\frac{1}{2}$  minim.

Dysmenorrhoea is well treated by 3 minim doses with 5 minims of tincture of belladonna thrice daily.

For examination nervousness a small dose thrice daily is a tonic.

**[P1] Mistura Gelsemii (R.L.O.H.).** Sodium salicylate 10 gr., sodium bicarbonate 10 gr., potassium bromide 10 gr., tincture of gelsemium 10 m., chloroform water to 1 oz. For neuralgia and generally as a sedative.

**[P1-81] Tinctura Gelsemii (B.P.C.).**

*Dose.*—5 to 15 minims (0.3 to 1 ml.). 1 in 10.

*Uses.* For neuralgia of face and jaws associated with carious teeth—15 m. every 6 hours may give relief. Is often given with ammonium or potassium bromide. In rheumatoid arthritis it is given with cimicifuga *g.v.* Disordered vision may follow even moderate doses.

INFLUENZA has been treated by the following:—Tincture of gelsemium 12 m., tincture of belladonna 5 m., potassium citrate 10 gr., syrup of orange 1 dr., chloroform water to 1 oz. *Dose.*—1 ounce every 4 hours. Afterwards  $\frac{1}{2}$  oz. until temperature falls to normal. Headache and backache vanish, with general improvement.

**[P1-81] Gelsemina (B.P.C.).**  $C_{20}H_{22}O_2N_2 = 322.2$ .

*Dose.*— $\frac{1}{100}$  to  $\frac{1}{30}$  grain (0.0005 to 0.002 g.) in pills.

Minute white crystals, m.p. 178°, with a bitterish taste, sparingly soluble in water, easily in alcohol, ether and acids. It forms crystalline salts, and has mydriatic properties, but it is now used only for trigeminal neuralgia.

**[P1-81] Gelseminæ Hydrochloridum.**  $C_{20}H_{22}O_2N_2.HCl = 358.7$ .

*Dose.*— $\frac{1}{100}$  to  $\frac{1}{30}$  grain (0.0005 to 0.002 g.).

In white, granular crystals, freely soluble in water.

**GENTIANA**

(with CALUMBA, QUASSIA, etc.)

*B.P., U.S.P. XI, Fr. Cx., P. Helv. V, P. Dan.*

*Dose.*—10 to 30 grains (0.6 to 2 g.).

The dried rhizome and roots of *Gentiana lutea* (Gentianaceæ). Ryutan (*P. Jap. V*) is obtained from *G. scabra*.

*Uses.* Gentian is a bitter tonic and is used to improve the appetite and to stimulate gastric secretion. It should be given from half to one hour before meals, since its administration with or after food is ineffective.

It is usually given with alkalis in conditions of hyposecretion, in chronic gastritis and atonic dyspepsia, in convalescence and in the dyspepsia of children.

**Extractum Gentianæ (B.P.).**

*Dose.*—2 to 8 grains (0.12 to 0.5 g.). A soft aqueous extract used as a pill excipient. *Fr. Cx.* has a soft extract prepared with alcohol 60%.

**Infusum Gentianæ Compositum Concentratum (B.P.).***Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Gentian about 1 in 10 with dried bitter orange peel and lemon peel in alcohol 25%.

**Infusum Gentianæ Compositum Recens (B.P.).***Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.).

Gentian 1 in 80 with dried bitter orange peel and lemon peel.

**Mistura Gentianæ Acida (B.P.C.).***Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.).

Contains 12 m. of dilute nitro-hydrochloric acid with syrup of orange, compound infusion of gentian and chloroform water to 1 oz.

*Mist. Gent. Acid. (N.I.F.).*Dilute hydrochloric acid 10 m., concentrated compound infusion of gentian 15 m., chloroform water to  $\frac{1}{2}$  oz.**Mistura Gentianæ Alkalina (B.P.C.).** *Syn.* MISTURA GENTIANÆ CUM SODA.*Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.).

Contains 15 gr. of sodium bicarbonate and 5 gr. of ammonium carbonate with syrup of orange and compound infusion of gentian to 1 oz.

*Mist. Sod. c. Gent. (N.I.F.).* *Syn.* MIST. GENT. ALK.Sodium bicarbonate 10 gr., concentrated compound infusion of gentian 15 m., water to  $\frac{1}{2}$  oz.*Tinctura Amara (P.G. VI).* Gentian 3, centaury root 3, orange peel 2, orange berries 1, zedoary root 1, diluted alcohol (67 to 69% v/v) to 50.**Tinctura Gentianæ Composita (B.P.).***Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.). Gentian 1 in 10 with dried bitter orange peel and cardamom in alcohol 45%.*Tinctura Gentianæ Composita (U.S.P. XI).**Average dose.*—60 minims (4 ml.).

Similar in composition to Tinct. Gent. Co. B.P., but contains also about 10% of glycerin.

*Azadirachta.* *Syn.* NIM or NEEM, MARGOSA. The bark of *Azadirachta indica* (Meliaceæ), indigenous to India. Used as a bitter instead of gentian or quassia.*Calamus (B.P.C.).* *Syn.* SWEET FLAG ROOT. *Dose.*— $\frac{1}{2}$  to 1 drachm (1 to 4 g.). The dried rhizome of *Acorus Calamus* (Araceæ). Aromatic bitter and carminative. *Tinctura Calami.* *Dose.*— $\frac{1}{2}$  to 1 drachm. 1 in 5. *Infusum Calami.* *Dose.*— $\frac{1}{2}$  to 1 ounce. 1 in 10.*Calumba (B.P., P. Helv. V, P. Dan., P. Jap. V).* *Syn.* RADIX FRASERI, COLOMBO (*Fr. Cx.*).The dried root, sliced, of *Jateorhiza palmata* (Menispermaceæ).

Bitter tonic for simple debility and indigestion. Contains no tannin and can be given with salts of iron.

False calumba root is from *Coscinium fenestratum*.*Infusum Calumbæ Concentratum (B.P.).* *Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.). About 1 in 2 $\frac{1}{2}$ .*Infusum Calumbæ Recens (B.P.).* *Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.). 1 in 20.

**Tinctura Calumbæ (B.P.).** *Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).  
1 in 10 of alcohol 60%. *Fr. Cx.* has 1 of drug to 5 of alcohol 60%.

**Cascarilla (B.P.C., P. Dan.).** The dried bark of *Croton Eluteria* (Euphorbiaceæ). Contains 1.5 to 2% of volatile oil, also the bitter principle cascarillin. Aromatic tonic.

**Infusum Cascarillæ Concentratum (B.P.C.).** *Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.). About 1 in 2 $\frac{1}{2}$ .

**Infusum Cascarillæ Recens (B.P.C.).** *Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.). 1 in 20.

[P1] **Mistura Cascarillæ Composita (St. T. H.).** Camphorated tincture of opium 15 m., vinegar of squill 20 m., emulsion of chloroform 10 m., infusion of cascarilla to 1 oz.

**Tinctura Cascarillæ (B.P.C.).** *Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.). 1 in 5.

**Chirata (B.P.C.).** The dried plant, *Swertia Chirata* (Gentianaceæ).

*Dose.*—5 to 30 grains (0.3 to 2 g.).

A bitter tonic given in indigestion for anorexia and torpid liver with constipation.

**Infusum Chiratæ Recens (B.P.C.).** *Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.). 1 in 20.

**Infusum Chiratæ Concentratum (B.P.C.).** *Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.). 1 in 2 $\frac{1}{2}$ .

**Tinctura Chiratæ (B.P.C.).**

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.). 1 in 10.

**Cimicifuga (B.P.C.).** *Syn.* BLACK SNAKEROOT, BLACK COHOSH, ACTÆÆ RACEMOSÆ RADIX.

*Dose.*—8 to 15 grains (0.5 to 1 g.).

The dried rhizome and roots of *Cimicifuga racemosa* (Ranunculaceæ).

**Uses.** *Cimicifuga* is a bitter tonic and has mild expectorant, anti-spasmodic and emmenagogue actions. It has been used internally in bronchitis, chronic rheumatism, lumbago, sciatica, chorea, dysmenorrhœa and amenorrhœa, usually in the form of the liquid extract or the tincture.

**Extractum Cimicifugæ Liquidum (B.P. '98).** *Dose.*—5 to 30 minims (0.3 to 2 ml.). 1 in 1.

**Tinctura Cimicifugæ (B.P.C.).** *Syn.* TINCTURA ACTÆÆ RACEMOSÆ.

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.). 1 in 10.

In rheumatoid arthritis 15 minims of tincture with 5 minims of tincture of gelsemium thrice a day is often useful.

**Cimicifugin.** *Dose.*—1 to 6 grains in pill. Is the resinous body obtained by pouring a strong tincture into water.

**Otosedan** (formerly known as *Otosclerol*) (Coates & Cooper, London). A preparation containing cimicifugin, bromides, and combined phosphorus. For deafness. *Dose.*—1 tablet thrice daily after meals, increased if necessary.

**Condurango (B.P.C., Fr. Cx., P. Jap. V, P.G. VI, P. Ital. V, P. Belg. IV, P. Helv. V, P. Dan.).**

*Dose.*— $\frac{1}{2}$  to 1 drachm (1 to 4 g.) in powder.

The stem bark of *Marsdenia Condurango* (Asclepiadaceæ) from Ecuador. Is bitter and acrid. A stomachic and stimulant in dyspepsia.

**Extractum Condurango Liquidum (P.G. VI)** is made 1 in 1 with alcohol 1 and water 3.

**Vinum Condurango** (P.G. VI). *Dose*.— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.). Liquid extract 10, aromatic tincture 1, sucrose 9, sherry 80. (*Tinctura Aromatica* (P.G. VI) is cinnamon 5, ginger 2, galanga 1, clove 1, cardamom 1, alcohol 69% v/v 50). *P. Jap. V* has a similar wine, but uses tincture of orange for aromatic tincture.

**Galanga** (B.P.C., *Fr. Cx.*, *P. Helv. V*, *P. Dan.*). *Syn.* LESSER GALANGAL, EAST INDIAN ROOT, CHINA ROOT.

*Dose*.— $\frac{1}{2}$  to  $\frac{1}{2}$  drachm (1 to 2 g.).

The dried rhizome of *Alpinia officinarum* (Zingiberaceæ). Aromatic and carminative. Has been used as decoction (1 in 20).

**Inula**. *Syn.* ELECCAMPANE. The dried rhizome and roots of *Inula Helenium* (Compositæ). Antiseptic; given internally in bronchitis as Extractum Inulæ Liquidum, 1 = 1, *dose*.—10 to 60 minims.

**Lupulus** (B.P.C.). *Syn.* HOPS, HOUBLON (*Fr. Cx.*), HUMULUS, STROBILI LUPULI.

The dried strobiles of the hop plant, *Humulus Lupulus* (Cannabaceæ). An aromatic bitter, formerly believed to possess sedative properties. The use of pillows stuffed with hops is reputed to induce sleep.

**Extractum Lupuli** (B.P.C.).

*Dose*.—5 to 15 grains (0.3 to 1 g.). A soft extract. A liquid extract, 1 in 1, *dose*.—5 to 15 minims, is also available.

**Infusum Lupuli Concentratum** (B.P.C.).

*Dose*.—1 to 2 drachms (4 to 8 ml.).

About 1 in 2 $\frac{1}{2}$ . This preparation diluted with 7 volumes of water may be dispensed when Infusum Lupuli is prescribed.

**Tinctura Lupuli** (B.P.C.).

*Dose*.— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.). 1 in 5.

**Lupulinum** (B.P.C., *P. Helv. V*).

*Dose*.—2 to 5 grains (0.12 to 0.3 g.) in pills, capsules or cachets.

A yellow powder, becoming brownish with age, consisting of the glandular trichomes from the strobiles of the hop plant.

**Menyanthes Trifoliata** (*Fr. Cx.*, *P. Dan.*). *Syn.* TRIFOLIA FIBRINA, BOG-BEAN LEAF, BUCKBEAN. Bitter tonic, emmenagogue, antiscorbutic, vermifuge and febrifuge; large doses are purgative and emetic; contains menyanthin, a glucoside. Infusion 1 in 20. *Dose*.—2 to 6 ounces, taken hot, early in the morning daily, useful for functional amenorrhœa. Liquid, extract with liquorice 1 in 2. *Dose*.— $\frac{1}{2}$  ounce.

**Quassia** (B.P., *Fr. Cx.*, *P. Helv. V*). *Syn.* JAMAICA QUASSIA.

*Dose*.—2 to 8 grains (0.12 to 0.5 g.).

Stem-wood of *Picræna excelsa* (Simarubaceæ). Contains picrosmin. Is free from tannin, hence compatible with iron preparations. *Surinam Quassia* (not now in use) is the wood of *Q. amara*, a branching shrub, whereas *P. excelsa* is about 100 feet high.

**Uses.** Quassia is mainly employed in medicine as a non-astringent bitter stomachic to stimulate appetite. A 1 in 20 infusion administered by rectal injection may be used in the treatment of threadworms; gelatin suppositories containing  $\frac{1}{4}$  to  $\frac{1}{2}$  gr. of the extract, and inserted on several successive nights, have also been employed for this purpose. Infusions have also been used as lotions for pediculosis.



Concentrated infusions or extracts are widely used, in conjunction with soft soap, as horticultural insecticides.

**Anti-smoking Gum.** Quassia made up in form of a chewing gum has been used as a substitute for smoking for the use of patients suffering from tobacco amblyopia who feel the loss of their tobacco. If alcoholic complication is absent 1 in 20 is strong enough.

**Enema Quassiae (B.P.C.).**

*Dose.*—20 ounces (600 ml.) of the fresh infusion.

**Extractum Quassiae (B.P.C.).**

*Dose.*—3 to 5 grains (0.2 to 0.3 g.). A soft extract.

**Infusum Quassiae Concentratum (B.P.).**

*Dose.*— $\frac{1}{4}$  to 1 drachm (2 to 4 ml.). 1 in 12 $\frac{1}{2}$ , extracted with cold water, and alcohol added.

**Infusum Quassiae Recens (B.P.).**

*Dose.*— $\frac{1}{4}$  to 1 ounce (15 to 30 ml.). 1%. Prepared with cold water.

[P2] **Lotio Quassiae.** Concentrated quassia infusion 1 oz., spirit of rosemary 1 $\frac{1}{2}$  dr., sassafras oil 30 m., alcohol 2 dr., liquefied phenol 2 dr., water to 6 oz. Shake before use. For nits in children's hair.

**Tinctura Quassiae (B.P.).** *Dose.*— $\frac{1}{4}$  to 1 drachm (2 to 4 ml.). 1% in alcohol 45%.

**Quassinum (Fr. Cx.)** *Syn.* PICRASMIN. A dry alcoholic extract in white odourless intensely bitter crystals. *Fr. Cx.* gives max. single dose, and *F.E. VIII* average dose,  $\frac{1}{16}$  grain.

[P1-S1] **Quebracha (B.P.C.).** *Syn.* QUEBRACHO, ASPIDOSPERMA, QUEBRACHO-BLANCO.

[P1] "*Alkaloids, the following; their salts, simple or complex:—Quebracho, alkaloids of, other than the alkaloids of red quebracho.*"

[S1] "*Alkaloids, the following; their salts, simple or complex:—Quebracho, alkaloids of.*"

[S6] "*Alkaloids—Quebracho, alkaloids of, other than the alkaloids of red quebracho—specify proportion as the proportion of any one alkaloid of quebracho that the preparation would be calculated to contain on the assumption that all the alkaloids of quebracho in the preparation were that alkaloid.*"

The dried bark of *Aspidosperma Quebracho* from Argentina. Tonic, febrifuge and antispasmodic. [P1-S1] Tincture of quebracho, 1 in 5, of alcohol 60%, *dose.*—1 drachm. [P1-S1] Liquid extract, 1=1, *dose.*—10 minims.

**Serpentaria (B.P., U.S.P. XI).**

*Dose.*— $\frac{3}{4}$  to 1 $\frac{1}{2}$  grains (0.05 to 0.1 g.). *U.S.P. XI* average dose 15 grains.

The dried rhizome and roots of *Aristolochia reticulata* (Texan Serpentry) (Aristolochiaceæ). A bitter tonic.

**Infusum Serpentariæ Concentratum (B.P.C.).**

*Dose.*— $\frac{1}{4}$  to 1 drachm (2 to 4 ml.).

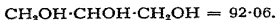
1 in 2 $\frac{1}{2}$ . When Infusum Serpentariæ is prescribed this preparation diluted with 7 times its volume of water may be dispensed.

**Tinctura Serpentariæ (B.P.C.).** *Dose.*— $\frac{1}{4}$  to 1 drachm (2 to 4 ml.). 1 in 5.

**Aristolochia (B.P.C.).** *Syn.* INDIAN BIRTHWORT, SAPSUN. The dried stem and root of *Aristolochia indica* (Aristolochiaceæ). A bitter used in the East for the same purpose as serpentary. Is administered as **Tinctura Aristolochiæ**, 1 in 5, *dose.*— $\frac{1}{4}$  to 1 drachm.

## GLYCERINUM

B.P., U.S.P. XI, Fr. Cx.



**Dose.**—1 to 2 drachms (4 to 8 ml.); by rectal injection,  $\frac{1}{2}$  to 2 drachms (2 to 8 ml.). U.S.P. XI average dose 60 minims.

**Intravenously,** 1 drachm (4 ml.) has been given with equal amount of tap water (*v. postea*).

**Manufactured** by decomposing fats with alkali or superheated steam. Sp. gr. 1.260 to 1.265. **Miscible** with water and alcohol 90%; but immiscible with ether or chloroform.

**P. Ned. V** permits 11.7 to 13.6% of water (sp. gr. 1.230 to 1.235). **Fr. Cx.** about 3% (sp. gr. 1.255); **P. Dan.** 12 to 15% (sp. gr. 1.225 to 1.235); **P. Helv. V** 12 to 16%. The latter includes also Glycerinum concentratum containing at least 98% of  $\text{C}_3\text{H}_8\text{O}_3$ . **U.S.P. XI** requires not less than 95%.

**CRYSTALLISATION** of glycerin occurs occasionally in the cold weather. The crystals do not melt again until temperature is about 20°.

**Uses.** Internally, glycerin is demulcent and laxative, and is widely employed as a sweetening agent in mixtures and as an ingredient in cough linctuses. Externally, it has little effect on the intact skin, but has a potent hygroscopic action when brought into contact with broken skin or mucous membranes. It is used as an emollient in many skin preparations and is of value in the prevention and treatment of chapped hands and chilblains, and it may be employed for its dehydrating effect in boils, carbuncles, and other inflammatory conditions, and as a wound dressing. Used in the form of tampons it has also proved of value, by promoting the flow of lymph, in the treatment of female gonorrhœa, and in leucorrhœa and chronic inflammation of the ovary, and intra-uterine injections of glycerin have been advocated in the treatment of puerperal sepsis and post-partum hæmorrhage. Given in the form of suppositories or by rectal injection, it is extensively employed in constipation, its irritant action on the mucous membrane causing prompt evacuation of the lower bowel.

It is a valuable preservative, especially in solutions of digestive ferments and other gland secretions, and is used for this purpose in extracts and in "aqueous" or non-alcoholic tinctures.

**BOILS AND CARBUNCLES,** and all kinds of wounds and sores, effectually treated; covered by gutta-percha tissue or oiled cambric. Also good in eczema. Absence of bleaching and maceration of the skin.—D. Kyle, *Brit. med. J.*, i/1931, 76.

**CELLULITIS.** Glycerin in combination with Liq. Hyd. Perchlor. excellent for all kinds.—H. A. Morton-Whitby, *Brit. med. J.*, i/1931, 206.

**TUBERCULOUS PERITONITIS** treated by glycerin 1 pint intraperitoneally—in desperate cases beneficial but toxic.—A. MacLennan. Probably diluted just as good.—D. Kyle, *Brit. med. J.*, i/1931, 76.

**Tuberculous abscess cavities** injected with glycerin after evacuation of contents and cauterising with iodised phenol.—H. A. Morton-Whitby, *Brit. med. J.*, i/1931, 206.

**VARICOSE VEINS.** Intravenous injections of 5 to 10 ml. of 50% glycerin and water initially, and 6 days later one or two injections of a 75% mixture. All cases successful.—F. Maignon, per *Prescriber*, 1932, 34.

**WOUNDS** as arriving in Casualty Dept. at a London hospital treated with a mixture of glycerin 1, liquid glucose 6 and water 3—left on 3 days, then a dry dressing with boric acid powder. Also effective in bromidrosis and in *ozæna*.—T. H. C. Benians, *Brit. med. J.*, i/1931, 285.

The addition of about 25% of glycerin to a wet dressing avoids the bleaching and maceration of the skin: the surface of the wound is kept moist, the discharge is not pent up under a scab and the wound is thus encouraged to heal from the bottom. Even when the dressing has to be applied for weeks or months the skin remains normal.—D. Kyle, *Practitioner*, ii/1933, 318.

#### Glycerin in Labour.

**LYMPHAGOGUE ACTION** of a 10% solution of tincture of iodine in glycerin. The iodine helps to stimulate uterine contraction.—H. J. Phillips, *Lancet*, ii/1925, 1229, 1307; *Proc. R. Soc. Med.*, Feb., 1926, 26.

In obstetrics glycerin is useful, (a) where puerperal sepsis is a possibility, and (b) mild sapremia or definite septicaemia.—C. Elliott, *Lancet*, i/1929, 1057.

Glycerin in midwifery advocated. It is powerfully hygroscopic, inhibits bacterial growth, particularly the cocci and coli groups, the causal organisms of puerperal sepsis, reduces oedema, and encourages healing of lacerated tissues. Soothing to hæmorrhoids. Used as routine at every confinement.—R. Mackinnon, *Brit. med. J.*, ii/1930, 980.

Glycerin and acriflavin (1 in 500) for torn perineum.—P. G. Preston, *Brit. med. J.*, i/1931, 294.

Glauramine (*q.v.*) in glycerin 1 in 60 suggested in midwifery, especially when frequent examinations needed and in prolonged or difficult labour. No irritation.—F. H. Lacey, *Brit. med. J.*, i/1931, 36.

Intravaginal glycerin of great value in sapremia—given twice daily for two days and then once daily till temperature drops, with elevation of the head of the bed a quarter of an hour after the glycerin has been given, and local heat. Also effective for septic tears of the perineum after labour, and after prolapse operations on the vagina (from the fifth day onwards). Intra-uterine injections of hot glycerin give good results in post-partum hæmorrhage. In salpingitis and gonorrhœal cervicitis vaginal glycerins are of assistance and preferable to hot douches.—W. McKim and H. McCullagh, *Brit. med. J.*, i/1939, 111.

**PUERPERAL SEPSIS.** Glycerin irrigation (up to 200 ml. once or thrice daily into the uterine cavity or cervical canal) the most effective remedy at our disposal, but should be used at an early stage. Pyrexia as a sign for puerperal sepsis an entirely unreliable guide—it rarely develops at the outset; pulse rate of more importance. Drainage by glycerin started as soon as temperature rises to 99° or pulse rate to 90. It is *not* normal for a woman to suffer from after-pains for the first few days after the puerperium, and pain is invariably due to interference with free drainage. Profuse lochial discharge another indication for early treatment.—A. R. Hobbs, *Brit. med. J.*, ii/1931, 746.

#### Enema Glycerini (B.P.C.).

**Dose.**— $\frac{1}{2}$  to 2 ounces (15 to 60 ml.). 20 to 50% *v/v* in water or mucilage of starch. Undiluted, 1 to 4 drachms (4 to 16 ml.).

#### Glycerinum Aluminis et Acidi Tannici.

Potassium alum (free from iron), in powder, 1, glycerin 6. Heat to dissolve and add tannic acid 1. An astringent throat pigment. Diluted 1 in 20 as a vaginal injection.

#### Glycerinum Boracis cum Potassii Chlorate (R.D.H.).

Potassium chlorate 20 gr., borax 10 gr., tragacanth 4 gr., glycerin 1 dr., chloroform water 1 oz.

#### Glycerinum cum Aqua Rosæ.

Glycerin 2, rose water 3. An agreeable emollient for the skin.

#### Glycerin Jelly, for toilet use.

Gelatin 140 gr., rose water 6 oz.; soak a few minutes and heat in a water-bath to dissolve; add, when cool but still fluid, white of egg  $\frac{1}{2}$  oz. Heat to coagulate completely, and add glycerin 6 oz., salicylic acid 12 gr. Mix well, filter through a hot-water funnel, and bottle while warm.

Non-greasy hand-creams may be made from tragacanth 2, glycerin 5, borax 1·25, tincture of benzoin 2·5, alcohol 4, distilled witch-hazel 3, perfume *q.s.*, water 81·75. Wet the tragacanth with the alcohol and add rapidly two-thirds of the water with continuous shaking; strain through muslin; add the tincture of benzoin mixed with the selected perfume. Dissolve the borax in the remainder of the water, add the glycerin and extract of witch-hazel, and mix the two solutions.—*Pharm. J.*, 1/1939, 556.

**Lubricant Glycerin Jelly** is somewhat softer than the latter. For toilet use and lubrication of stomach tubes.

**Glycero-alcohol.** *Syn.* PETIT'S LIQUOR.

*Dose.*—5 to 60 minims (0·3 to 4 ml.).

Glycerin 333, distilled water 146, alcohol 95% 580. Is used as a solvent of alkaloids and active principles. It has sp. gr. about 1.

**Suppositorium Glycerini (B.P.).** Gelatin 14, glycerin (by weight) 70, water *q.s.* to 100, suitably combined. Pour into moulds of 15, 30, 60 or 120 minims or other capacities as required. Contains 70% by weight of glycerin. This basis may be used for gelatin pessaries.

**Suppositorium Glycerini Saponatum (B.P.C.)** contains 90% *w/w* of glycerin.

**Suppositoria Glycerini (U.S.P. XI).**

Dissolve 8 g. of sodium stearate in 92 g. of glycerin heated at 95°, add 5 g. of water and pour into moulds to produce 30 suppositories.

**Glycerin Tampons** consist of gauze and wool swabs soaked in medicated glycerin.

**Hollow Suppositories**, composed of oil of theobroma, may be filled with 20, 45, or 90 grains of glycerin; they are prompt in action.

**Unguentum Glycerini Compositum (St. T. H.).**

Glycerin 3 dr., strong solution of lead subacetate 20 m., wool fat 3 dr., lavender oil 1 m., yellow soft paraffin to 1 oz.

## Glycols.

The glycols are dihydric alcohols with a general formula  $\text{HO}\cdot\text{R}_1\cdot\text{R}_2\cdot\text{OH}$ , where  $\text{R}_1$  and  $\text{R}_2$  represent any alkyl groups either similar or dissimilar. In ethylene glycol,  $\text{HO}\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{OH}$ , for example, they are similar, whereas in  $\alpha$ -iso-amylene glycol,  $\text{HO}\cdot\text{CH}_2\cdot\text{CH}[(\text{CH}_3)_2]\cdot\text{OH}$ , they are dissimilar. By condensing together two molecules of glycol, either similar or dissimilar, a compound is obtained which, whilst being a dihydric alcohol, is also an ether, such as diethylene glycol,  $\text{HO}\cdot\text{C}_2\text{H}_4\cdot\text{O}\cdot\text{C}_2\text{H}_4\cdot\text{OH}$ . In addition to this "internal ether," condensation ethers may be formed by replacing either or both of the hydrogen atoms of the hydroxyl groups. In this way ethyleneglycol-monoethylether,  $\text{C}_2\text{H}_5\text{O}\cdot\text{CH}_2\cdot\text{CH}_2\text{OH}$ , is obtained.

Very few glycols, with the exception of propylene glycol, are used in pharmaceutical preparations, but large quantities are used in the cosmetic and other industries, and glycols as a class show a toxicity which, although seemingly negligible in some members, may nevertheless prove detrimental to health in the long run, owing to the cumulative effect of the toxic principle. The nature of this principle is unknown and may be due either to the presence of a cyclic ether in the product before ingestion, or to its formation

actually in the body. Whichever glycol is used in a preparation, care should be taken to determine its toxicity prior to use.

**Ethylene Glycol.** *Syn.* GLYCOL.  $\text{CH}_2\text{OH}\cdot\text{CH}_2\text{OH} = 62.07$ .

Ethylene glycol is a colourless, odourless, syrupy liquid with a sweet taste. Its properties are intermediate between those of alcohol and glycerin. M.p.  $-17.4^\circ$ , b.p. about  $197^\circ$ .

**Miscible** with water and alcohol; soluble 1 in about 200 of ether.

Ethylene glycol is used as a solvent, particularly for preparing flavouring essences; it is a good solvent for terpeneless oils. It is also used as an "anti-freeze," and as an ingredient in dynamite. Ethylene glycol is non-inflammable and non-corrosive to metals.

As a solvent or vehicle for medicinal products it is comparatively innocuous. It is said that even 140 ml. would be needed to cause toxic symptoms in man, and the fatal dose would be more than  $\frac{1}{2}$  lb.—P. J. Hanzlik and co-workers, *J. Pharmacol.*, Apr., 1931, 406. W. F. von Oettingen and E. A. Jirouch, *ibid.*, Aug., 1931, 371, draw, however, other conclusions and say subcutaneously likely to cause irritation and large doses may cause severe gastro-enteritis.

Ethylene and propylene glycols are both more effective preservatives for solutions of tannic acid than either alcohol or glycerin. In 10% concentration they are effective in preserving syrup and suspensions of tragacanth, and a 30% concentration is a satisfactory preservative for solutions of gelatin.—J. Rae, *Pharm. J.*, i/1938, 517.

**Propylene Glycol.**  $\text{CH}_3\cdot\text{CHOH}\cdot\text{CH}_2\text{OH} = 76.09$ .

Propylene glycol is a clear, colourless, odourless, hygroscopic liquid obtained by the hydrolysis of propylene chloride. It is less viscous than glycerin and should be stored in well-closed containers.

**Miscible** with water, alcohol and chloroform; soluble 1 in 10 of ether; immiscible with fixed oils.

This is the least toxic of the glycols, and may safely be employed as a vehicle or solvent in medicinal preparations.

**Toxicity.** The M.L.D. of propylene glycol (1:2-propanediol) intramuscularly and subcutaneously for rats is 15.7 and 23.1 g. per kg. respectively as compared with 7.6 and 15.1 g. per kg. respectively for glycerin. The acutely fatal oral dose for rabbits is 20 g. per kg. Daily doses of up to 8 ml. per kg. for 50 days produce no cumulative effects. Its subcutaneous injection into human subjects causes a marked burning sensation which passes off in 5 to 10 minutes. It should be a useful solvent for certain substances but should not be given undiluted by subcutaneous injection.—H. A. Braun and G. F. Cartland, *J. Amer. pharm. Ass.*, 1936, 746.

With the exception of propylene glycol, the use of glycols in food and drug preparations should be avoided.—H. O. Calvery, per *J. Amer. pharm. Ass.*, 1939, 6.

Although very large doses of the propylene and dipropylene glycols act as central nervous depressants, these glycols are devoid of demonstrable toxicity when administered in smaller though still large doses for prolonged periods. With doses of a glycol which might conceivably be ingested by man, the propylene and dipropylene glycols showed no evidence of toxicity. Only propylene glycol is suitable at present for internal or systemic use with food and medicinal products without demonstrable hazards to health.—P. J. Hanzlik *et al.*, *J. Pharmacol.*, 1939, 67, 101.

Has no demonstrable effects on the basal metabolic rate in human subjects (50 ml. in a 50% aqueous solution *per os*) and on the respiratory quotient in rats. This is further evidence in support of its non-injuriousness as a vehicle or solvent, if not desirability as an alcohol substitute in dietary and medicinal products.—P. J. Hanzlik, *J. Pharmacol.*, 1939, 67, 114.

Further confirmation that this is the least toxic and injurious of the glycols thus far investigated.—W. Van Winkle and N. K. Kennedy, *J. Pharmacol.*, 1940, 69, 140.

**$\alpha$ -Propyleneglycol Monostearate.** *Syn.* MONOLENE. A wax-like solid containing traces of the distearate and having a m.p. of 33° to 34° when fresh, rising to 37° on storage. Suggested for use as a suppository basis, and stated to favour the absorption of water soluble medicaments.—J. C. Bird, *J. Amer. pharm. Ass.*, 1937, 475.

**Diethylene Glycol.**  $(\text{CH}_2\text{OH}\cdot\text{CH}_2)_2\text{O} = 106.12$ .

Diethylene glycol, or  $\beta$ ,  $\beta'$ -dihydroxydiethyl ether, is a colourless, hygroscopic, odourless, oily liquid, with a sweet taste, made by heating ethylene oxide and glycol. B.p. 245°. Soluble in water, alcohol and ether; insoluble in benzene and carbon tetrachloride.

Diethylene glycol is used for many technical purposes. Mixed with 60% of water, it freezes at -18°, and with 50% at -28°, and is thus used as an "anti-freeze." It is not used medically owing to its toxicity. (For references to toxicity see Vol. II, 21st Edn.)

**Ethyleneglycol Monoethylether.** *Syn. and Prop. Name.* MONOETHYL ETHYLENEGLYCOL, CELLOSOLVE (*Carbide and Carbon Chemicals, New York*).  $\text{C}_2\text{H}_5\text{O}\cdot\text{CH}_2\cdot\text{CH}_2\text{OH} = 90.12$ .

Ethyleneglycol monoethyl ether is a colourless, odourless liquid. B.p. 135°; flash point 44°. Miscible with water and organic solvents. It dissolves many oils, resins, waxes, etc.

Used as a solvent for cellulose nitrate, etc., and in varnish removers and dye baths. It is also used in cosmetic creams.

**Diethyleneglycol Monoethylether.** *Syn. and Prop. Name.* MONOETHYL DIETHYLENEGLYCOL, CARBITOL (*Carbide and Carbon Chemicals, New York*).  $\text{C}_2\text{H}_5\text{O}\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{O}\cdot\text{CH}_2\cdot\text{CH}_2\text{OH} = 134.17$ .

Diethyleneglycol monoethyl ether is a colourless, hygroscopic liquid. B.p. 200°. Miscible with water and organic solvents.

It is used as a solvent for cellulose nitrate and resins, and also in cosmetic creams.

## GLYCYRRHIZA

*B.P., U.S.P. XI, Fr. Cx., P. Helv. V, P. Dan.*

**Dose.**—15 to 60 grains (1 to 4 g.).

The root and subterranean stem of *G. glabra* and other species (Leguminosæ). Both the peeled and unpeeled drug is included in the *B.P.*, the latter being admitted only when expressly named, e.g., for preparing the extracts. Is demulcent and expectorant.

**Elixir Glycyrrhizæ (U.S.P. XI).**

Fluid extract of glycyrrhiza 12.5%, in aromatic elixir.

**Liquor Pectoralis (P. Dan.).** *Syn.* ELIXIR PECTORALE, KING OF DENMARK'S CHEST MIXTURE. **Dose.**—1 drachm. Extract of liquorice 1, fennel water 3, anisated liquid ammonia 1.

**P. Sec. X** has extract of liquorice 200, fennel water 600, ammonia solution 9% 35, anise oil 2, alcohol 90% 163. [**P. I**] **Liquor Pectoralis Benzoicus (P. Sec. X).** Tinctura Opii Benzoica 1, Liquor Pectoralis 3.

**Extractum Glycyrrhizæ (B.P.).**

**Dose.**—10 to 30 grains (0.6 to 2 g.).

The evaporated chloroform water percolate. Used in lozenges and pastilles.

**Extractum Glycyrrhizæ (U.S.P. XI).** This is the commercial extract in powder or in rolls or masses. **Extractum Glycyrrhizæ Purum (U.S.P. XI)** is an aqueous extract of the rhizome and roots, of pilular consistence.

**Extractum Glycyrrhizæ Liquidum (B.P.).**

**Dose.**— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

1 in 1, by percolation with chloroform water, evaporation, and addition of 25% of alcohol 90%. Is a useful flavouring agent, especially for ammonium chloride, alkaline iodides, cascara, magnesium sulphate, quinine sulphate, ipecacuanha and aloes, but is incompatible with acids.

**Extractum Glycyrrhizæ** (*Fr. Cx.*). *Syn.* EXTRAIT DE RÉGLISSE.

Made by double maceration with very dilute ammonia and evaporation to a soft extract.

**Fluidextractum Glycyrrhizæ** (*U.S.P. XI*).

*Average dose.*—30 minims (2 ml.). Prepared by maceration and percolation with boiling water, followed by evaporation after the addition of ammonia and then finally adding alcohol and sufficient water.

**Pulvis Glycyrrhizæ Compositus** (*B.P.*). *Syn.* PULVIS PECTORALIS (*Kurellæ*).

*Dose.*—1 to 2 drachms (4 to 8 g.) mixed with water or milk, taken early in the morning.

Senna and liquorice of each 2, fennel and sublimed sulphur of each 1, sucrose 6½. Mix. For constipation and hepatic disease, it is pleasant to take, and effectual without catharsis. *U.S.P. XI* (*Pulvis Sennæ Compositus*) uses oil of fennel, which makes it less granular, and 3% of the sugar may be replaced by starch.

**Poudre de Réglisse Composée** (*Fr. Cx.*). *Syn.* PULVIS LIQUIRITIZÆ COMPOSITUS. Contains liquorice 1½, senna (washed with alcohol and powdered) 1½, fennel 1, sublimed sulphur 1, sucrose 5. *P. Jap. V* is similar.

**Pulvis Sennæ Compositus** (*U.S.P. XI*). *Syn.* PULVIS GLYCYRRHIZÆ COMPOSITUS (*U.S.P. X*).

*Average dose.*—60 grains (4 g.).

Senna 18, liquorice 23·6, washed sulphur 8, oil of fennel 0·4, sucrose 50.

**Trochisci Glycyrrhizæ** (*B.P.C.*), *syn.* BROMPTON COUGH LOZENGES, contain 3 grains of extract of liquorice and ½ minim of oil of anise. These lozenges are brown in colour. Lozenges which are black usually contain charcoal.

**Pastilles de Réglisse.** Liquorice pastilles, much used in France.

**Glycyrrhizinum Ammoniatum.** *Dose.*—½ to 5 grains. Glycyrrhizin is contained in the root as the ammonium salt. Readily soluble garnet coloured shining scales. It possesses a persistent sweet taste. A grain will flavour 6 ounces of water. It may, perhaps, be considered as the ammonium salt of glycyrrhizinic acid which, according to Tschirch, has the formula  $C_{41}H_{61}O_{23}(COOH)_2$ .

In addition to the extracts, dried "liquorice juice," or "Spanish liquorice" (*Succus Liquiritizæ*, *P. Helv. V*) is sold, that bearing the stamp of Solazzi being most prized. Pontefract cakes of liquorice and "pipe liquorice" are useful in allaying tickling coughs.

**Abrus** (*B.P.C.*). *Syn.* JEQUIRITY, JUMBLE BEADS, PRAYER BEADS.

The seeds of *Abrus precatorius* (*Leguminosæ*), a tropical climbing plant. Contains abrin, a mixture of two poisonous proteins. Infusum Abri 8% has been used, diluted, for granular eyelids.

Instillation of 5% infusion of crushed seeds for relief of pannus.—Lieut.-Col. H. Kirkpatrick, *Lancet*, i/1921, 1304.

**Abri Radix**, *syn.* INDIAN LIQUORICE, is the root of *Abrus precatorius* (*Leguminosæ*). It has poisonous properties and should not be used as a sweetening agent.

**Althæa** (*B.P.C.*, *U.S.P. XI*, *P. Dan.*). *Syn.* MARSHMALLOW, GUIMAUVE (*Fr. Cx.*).

The dried peeled root of *A. officinalis* (*Malvaceæ*), collected from plants not less than two years old. Contains a fatty oil and

25 to 35% of mucilage. Used as a demulcent in bronchitis. The powdered root is a useful absorbent in pill-making. The leaves (*Althææ Folium P. Helv. V*) were formerly used for preparing a soothing ointment.

**Marshmallow Pastilles.** *Syn.* PASTILLES DE GUIMAUVE.

Boil incised marshmallow root 100 in water 400, strain off the liquor. Evaporate to about 80 and mix with tragacanth 10 and sugar 1000, adding orange-flower water 10 or more if necessary to make a mass for cutting into pastilles weighing 20 grains (1.2 g.). This basis may be medicated with throat remedies similar to those used in glyco-gelatin pastilles.

**Species Pectorales (P.G. VI).** Coarsely cut marshmallow root 8, liquorice root 3, orris root 1, tussilago farfara (coltsfoot) leaves 4, verbascum flowers 2, anise 2.

**Syrupus Althææ (B.P.C.).** *Syn.* SYRUP OF MARSHMALLOW.

*Dose.*— $\frac{1}{2}$  to 2 drachms (2 to 8 ml.). 1 in 25.

**Cetraria (B.P.C., P. Helv. V, P. Dan.).** *Syn.* LICHEN D'ISLANDE (*Fr. Cx.*).

Iceland moss is the dried lichen, *C. islandica* (Parmeliaceæ.) Contains the carbohydrate, lichenin, and its isomeride iso-lichenin. Has demulcent properties, and is used in Northern Europe as a food.

Usually administered as *Decoctum Cetrariæ*, dose—1 to 4 fl. ounces (30 to 120 ml.), 1 in 20; also as lozenges, the bitterness (due to cetraric acid) being removed by prolonged soaking in water.

**Marrubium (B.P.C.).** *Syn.* HOREHOUND.

*Dose.*— $\frac{1}{2}$  to  $\frac{1}{2}$  drachm (1 to 2 g.). The dried leaves and flowering tops of *M. vulgare* (Labiatae). Expectoant, laxative in large doses.

**Infusum Marrubii Concentratum (B.P.C.).** *Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.). 1 in 2 $\frac{1}{2}$ . This preparation diluted with 7 volumes of water may be dispensed when Infusum Marrubii is prescribed.

**Syrupus Marrubii (B.P.C.).** *Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.). About 1 in 2. Prepared by dissolving sucrose in an aqueous decoction of the drug.

**Symphytum (B.P.C.).** *Syn.* COMFREY ROOT.

The dried rhizome and root of *Symphytum officinale* (Boraginaceæ). Contains 0.6 to 0.8% of allantoin, and has been applied to wounds and ulcers in form of a decoction (1 in 20), or as a poultice prepared from the fresh root. The liquid extract (1 in 4 by extracting the drug in coarse powder with water, and preserving with 20% of 90% alcohol) has been given internally for gastric ulcer in doses of 2 to 4 drachms.

"An ancient remedy and its modern utilities. The *Symphytum officinale* and its contained allantoin." By C. J. Macalister. Together with an account of the chemical constitution of allantoin. By A. W. Titherley (*John Bale, Sons & Danielsson*, 1936).

**Allantoinum (B.P.C.).**  $C_4H_8O_3N_4 = 158.1$ .

*Dose.*— $\frac{1}{2}$  to 2 grains (0.03 to 0.12 g.).

A diuretic of glyoxylic acid, occurring to the extent of about 0.8% in comfrey. It is prepared synthetically by the oxidation of uric acid. Occurs in colourless crystals. M.p. about 235°.

**Soluble** 1 in about 200 of water, almost insoluble in alcohol 90%, and ether.



A cell proliferant. Has been applied locally to indolent ulcers and sluggish wounds and abscesses.

The activity of allantoin has been stated to be due to the formation of urea.—per *J. Amer. med. Ass.*, ii/1938, 758.

**Tussilaginīs Flos** (*B.P.C.*, *Fr. Cx.*). *Syn.* COLTSFOOT FLOWER, FARFARÆ FLORES. The dried flowering shoots of *Tussilago Farfara* (*Compositæ*). Demulcent, relieves irritable cough.

**Extractum Tussilaginīs Liquidum** (*B.P.C.*). *Syn.* LIQUID EXTRACT OF COLTSFOOT.

*Dose.*—10 to 30 minims (0.6 to 2 ml.). 1 in 1.

**Syrupus Tussilaginīs** (*B.P.C.*). *Syn.* SYRUP OF COLTSFOOT.

Liquid extract of coltsfoot 25% *v/v* in syrup.

**Tussilaginīs Folium** (*B.P.C.*). *Syn.* FARFARÆ FOLIA.

The dried leaves of *Tussilago Farfara*. Has been administered for its demulcent properties in the form of a decoction (1 in 20, *dose.*—2 ounces).

## GOSSYPHII CORTEX

### *B.P.C.*

#### *Syn.* GOSSYPHII RADICIS CORTEX.

The root bark of *Gossypium herbaceum* (*Malvaceæ*) and other cultivated species.

**Uses.** Has been used as an emmenagogue and abortifacient. May relieve dysmenorrhœa.

**Decoctum Gossypii Corticis** (*B.P.C.*). *Dose.*— $\frac{1}{2}$  to 2 ounces (15 to 60 ml.). 1 in 5.

**Extractum Gossypii Corticis Liquidum** (*B.P.C.*).

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.). 1 in 1.

**Tinctura Gossypii Corticis** (*B.P.C.*). 1 in 4.

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

**Lactagol** (*Lactagol, London; Pearson, Mitcham*) is an extract of cotton seed. *Dose.*—1 teaspoonful 4 or 5 times daily given in milk.

Used to increase the flow of milk and the nitrogenous constituents of same. **Edestine.** Stated to be the active principle, so far as galactagogue action is concerned, of cotton seed freed from fat, etc. Is also obtainable from linseed by precipitation with water from a 4% saline extractive.

**Aletris** (*B.P.C.*). *Syn.* STAR GRASS, AGUE ROOT, COLIC ROOT. (*Dioscorea* is also called colic root).

The dried rhizome and roots of *A. farinosa* (*Liliaceæ*). Used as a so-called uterine tonic.

**Elixir Aletridis** (*B.P.C.*). *Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

A flavoured preparation containing 25% *v/v* of liquid extract of aletris.

**Extractum Aletridis Liquidum** (*B.P.C.*). *Dose.*—5 to 15 minims (0.3 to 1 ml.). 1 in 1.

**Caulophyllum** (*B.P.C.*). *Syn.* BLUE COHOSH, PAPOOSE OR SQUAW ROOT. *Dose.*—5 to 30 grains (0.3 to 2 g.).

The rhizome and roots of *C. thalictroides* (*Berberidaceæ*).

Diuretic and emmenagogue.

**Extractum Caulophylli Liquidum (B.P.C.).** Dose.—10 to 30 minims (0.6 to 2 ml.). 1 in 1.

**Liquor Caulophylli et Pulsatillæ (B.P.C.).** Dose.—1 to 2 drachms (4 to 8 ml.).

Contains 25% v/v of liquid extract of caulophyllum and 5% v/v of liquid extract of pulsatilla.

**Liquor Caulophylli et Pulsatillæ Compositus (B.P.C.).**

Dose.—1 to 2 drachms (4 to 8 ml.).

Contains liquid extracts of caulophyllum 15%, pulsatilla 5%, aletris 10%, and black haw 20% (all by volume). A sedative in dysmenorrhœa and uterine disorders.

**Caulophyllin, dose.**—1 to 4 grains (0.06 to 0.25 g.), is the resinoid obtained by precipitating a concentrated alcoholic tincture. Has diuretic, diaphoretic, anthelmintic, antispasmodic and emmenagogue properties.

**Helonias. FALSE UNICORN ROOT.** The dried rhizome and root of *Chamoelirium luteum*. Is used in colic and in atony of the generative organs; also employed as an abortifacient.

**"Helonias Compound."** Aloes 9 oz., helonias 14 oz., tansy 14 oz., oil of pennyroyal 1½ oz., oil of cassia 1 drachm, cayenne ½ oz., myrrh 8½ oz. in 1 gallon of 17% alcohol. Dose.—1 drachm in a cup of hot water, sweetened, twice daily. For promoting menstruation.

**Piscidia (B.P.C.). Syn. JAMAICA DOGWOOD.** The root bark of *P. Erythrina* (Leguminosæ). Useful in neuralgia, toothache, bronchitis, pertussis, insomnia, and dysmenorrhœa.

**Extractum Piscidiæ Liquidum (B.P.C.).** Dose.—½ to 2 drachms (2 to 8 ml.). 1 in 1. A dry alcoholic extract, dose—2 to 5 grains, is also prepared.

**Pulsatilla (B.P.C., Fr. Cx.). Syn. PASQUE FLOWER.** The dried herb, *Anemone Pulsatilla* (Ranunculacæ). Contains a crystalline vesicant substance, anemone camphor. Fr. Cx. specifies fresh flowering plant. Used in dysmenorrhœa and amenorrhœa.

**Extractum Pulsatillæ Liquidum (B.P.C.).** Dose.—2 to 5 minims (0.12 to 0.3 ml.). 1 in 1.

**Tinctura Pulsatillæ (B.P.C.).** Dose.—5 to 30 minims (0.3 to 2 ml.). 1 in 10.

Dysmenorrhœa may be relieved by the following mixture: Tinct. Pulsatilla 4 dr., Spt. Chlorof. 2 dr., chloroform water to 6 oz. 2 dr. to be taken as soon as menstrual (or premenstrual) pain begins and every three hours while pain continues.

**Senecio. RAGWORT.** *Senecio Jacobæa* and *S. aureus* (Compositæ) are emmenagogues, and have been employed in amenorrhœa and dysmenorrhœa. Liquid Extract, 1 = 1 of herb. Dose.—20 to 60 minims. *Senecio cineraria* (*Cineraria maritima*) has been employed in the form of a tincture, 3 to 4 drops to an eye-bath of water, in the treatment of cataract. The fresh juice has also been used as eye-drops for the same purpose.

**Viburnum (B.P.C., Fr. Cx., P. Helv. V). Syn. BLACK HAW.** Dose.—½ to ½ drachm (1 to 2 g.).

The dried root bark of *V. prunifolium* (Caprifoliacæ). Anti-spasmodic, diuretic and nervine sedative. Used in dysmenorrhœa and in threatened abortion for its supposed sedative effect on the uterus.

**Elixir Viburni (B.P.C.). Syn. ELIXIR VIBURNI PRUNIFOLII.**

Dose.—½ to 2 drachms (2 to 8 ml.). Liquid extract of black haw 1 in 8 with compound tincture of cardamom and aromatic elixir.

**Elixir Viburni et Hydrastis (B.P.C.). Syn. ELIXIR VIBURNI COMPOSITUM.**

Dose.—½ to 1 drachm (2 to 4 ml.).

Contains liquid extract of black haw 30 m. and extract of hydrastis about 1 gr. in 1 dr.

**Extractum Viburni (B.P.C.).** *Dose.*—3 to 8 grains (0.2 to 0.5 g.). A soft extract.

**Extractum Viburni Liquidum (B.P.C., Fr. Cx.).** *Dose.*—1 to 2 drachms (4 to 8 ml.). 1 in 1.

## GOSSYPIMUM

### AND OTHER ALLIED DRESSINGS.

*For descriptions of medicated surgical dressings, see under individual medicaments (also Index).*

*By rule 10 of the Poisons Rules, 1935, the provisions of the Pharmacy and Poisons Act, 1933 and of the Poisons Rules, 1935, which apply solely to substances included in the First Schedule to the Poisons Rules do not apply to surgical dressings.*

**Gossypium Absorbens (B.P.C.).** *Syn.* ABSORBENT COTTON WOOL, GOSSYPIMUM DEPURATUM (*P. Helv. V, Fr. Cx.*), GOSSYPIMUM PURIFICATUM (*U.S.P. XI*). The prepared epidermal trichomes of the seeds of various species of *Gossypium* (*Malvaceæ*). The filaments each consist of a single cell 2 to 4 cm. long forming a flattened tubular band. It is required to be not more neppy than a standard sample, and to comply with a test for absorbency. *U.S.P. XI* requires absorbent cotton to comply with tests for sterility. Cotton wool is soluble in an ammoniacal solution of copper oxide.

**Curatio Normalis XIII (B.P.C. Supp.).** *Syn.* STANDARD DRESSING No. 13, SMALL PLAIN WOUND DRESSING.

The dressing consists of a pad sewn to an open-weave bandage measuring 2 inches by 2½ yards. The pad, which measures 4 inches by 3 inches, is composed of about 100 gr. of absorbent cotton wool enclosed in absorbent gauze. The gauze, which is 4 inches long, is either woven tubular 6½ inches in circumference, or woven single width 8 inches wide.

**Curatio Normalis XIV (B.P.C. Supp.).** *Syn.* STANDARD DRESSING No. 14, MEDIUM PLAIN WOUND DRESSING.

This dressing is similar to Standard Dressing No. 13, but the pad measures 6 inches by 4 inches, and is composed of about 200 gr. of absorbent cotton wool enclosed in absorbent gauze 6 inches long, and either woven tubular 9 inches in circumference, or woven single width 10 inches wide. The open-weave bandage measures 2½ inches by 3 yards.

**Curatio Normalis XV (B.P.C. Supp.).** *Syn.* STANDARD DRESSING No. 15, LARGE PLAIN WOUND DRESSING.

This dressing is similar to Standard Dressing No. 13, but the pad measures 8 inches by 6 inches, and is composed of about 400 gr. of absorbent cotton wool enclosed in absorbent gauze 8 inches long, and either woven tubular 13 inches in circumference, or woven single width 14 inches wide. The open-weave bandage measures 3 inches by 4 yards.

**Bandages** are made termed black cloth, buttercloth, calico, "cataract" (of special form for bandaging after the operation), crêpe, crêpe (Velpau), crinoline (for silicating and plaster of Paris), domette, elastic circular stocking (stockinette), elastic (india-rubber webbing), flannel, gauze, muslin (for plaster of Paris), open wove (absorbent), plaster of Paris, selvedge (white and grey) and triangular splint.

**Ligamentum Crispi (B.P.C.).** *Syn.* CRÊPE BANDAGE. A characteristic fabric of plain weave in which the warp threads are of cotton and wool, and the weft threads are entirely of cotton. When fully extended the length is not less than twice the unstretched length, and after being stretched for 1 minute it returns to not more than two-thirds the fully-extended length.

**Ligamentum Domettæ (B.P.C.).** DOMETTE BANDAGE. A union fabric of plain weave in which the warp yarns are of cotton and the weft yarns of wool.

**Ligamentum Lanulæ (B.P.C.).** FLANNEL BANDAGE. A raised fabric of plain weave made entirely of wool.

**Ligamentum Linæ (B.P.C.).** BLEACHED CALICO BANDAGE. A bleached cotton cloth of plain weave.

**Ligamentum Linæ Crudum (B.P.C.).** UNBLEACHED CALICO BANDAGE. An unbleached cotton cloth of plain weave.

**Ligamentum Sindonis (B.P.C.).** MUSLIN BANDAGE. A cotton cloth of plain weave known as butter cloth material.

**Ligamentum Textum Apertum (B.P.C.).** OPEN-WOVE BANDAGE. *Syn.* WHITE OPEN-WOVE BANDAGE. Cotton cloth of plain weave.

**Battista (B.P.C.).** BATTISTE. A bleached cotton fabric proofed on both surfaces with a rubber solution rendering it impervious to water and forming a non-adhesive surface. It is heat vulcanised and not cold cured.

**Billroth's Cambric.** Cotton fabric treated by a special process. It takes the place of gutta-percha tissue and oiled silk, being sterilisable.

**Carbasus Absorbens (B.P.C.).** ABSORBENT GAUZE. *Syn.* UN-MEDICATED GAUZE. Cotton cloth of plain weave containing per inch not less than 19 threads in the warp and not less than 15 in the weft. It complies with a test for absorbency.

**Carbasus Absorbens in Tænia (B.P.C.).** ABSORBENT RIBBON GAUZE. A material similar to the preceding but containing per inch not less than 30 threads in the warp and not less than 35 in the weft.

The following medicated ribbon gauzes are made in  $\frac{1}{4}$ ,  $\frac{1}{2}$ , 1 and 2-inch widths, in 12 yard lengths:—Alembroth, aluminium acetate, boric acid, iodoform, [P1] mercury and zinc cyanide, [P2] mercuric chloride, [P2] phenol.

**Tulle Gras (Lumière, Paris; Anglo-French Drug Co., London).** Surgical dressing consisting of wide-mesh gauze impregnated with soft paraffin and 1% balsam of Peru, and sterilised.

For the treatment of burns on the face and hands the Ministry of Health recommends (1941) the use in the Emergency Medical Services of Tulle Gras (not tannic acid). Similar emergency treatment is also recommended for serious burns in other parts of the body (prior to coagulation treatment).—*Pharm. J.*, i/1941, 77.

**Nonad Tulle (Allen & Hanburys, London), Jelonet (Smith & Nephew, Hull) and Optrex Tulle (Optrex Ltd., London C. F. Thackray, Leeds)** are similar preparations.

A dressing similar to Tulle Gras may be prepared in the following way. Curtain net, with a mesh of 2 mm. is cut into pieces 9 cm. square. These are

placed in a metal box slightly larger in size. The box is then filled with the following mixture: soft paraffin 96 g., balsam of Peru 2 g., halibut oil 2 g., sufficient to impregnate and cover the material completely after sterilisation.—A. H. McIndoe, *Proc. R. Soc. Med.*, 1940, 34, 62.

**Cellulosum Ligni (B.P.C.).** CELLULOSE WADDING. *Syn.* TILLMAN'S DRESSING. Is prepared from high-grade bleached sulphite pulp and complies with a test for absorbency.

**Charta Oleata (B.P.C.).** OILED PAPER.

White paper rendered waterproof by treatment with a drying oil.

**Jaconettum (B.P.C.).** JACONET. A bleached cotton fabric, proofed on one side with a rubber solution rendering it impervious to water and forming a non-adhesive surface. It is heat vulcanised and not cold cured. Pink jaconet, coloured with a suitable dye, is also available.

**Lana (B.P.C.).** *Syn.* ANIMAL WOOL, LAMB'S WOOL. Wool is the fleece of the sheep prepared by cleansing to remove grease and other foreign substances. It consists of solid cylindrical hairs soluble in 4.5% aqueous sodium hydroxide, insoluble in ammoniacal copper oxide solution which stains it blue.

**Linteum Absorbens (B.P.C.).** ABSORBENT LINT. *Syn.* LINT, COTTON LINT, UNMEDICATED LINT, LINTEUM CARPTUM. A cotton cloth of plain weave from the warp yarns of which a nap has been raised. It complies with a test for absorbency.

Lint is also obtainable medicated with iodoform 10%, and with ferric chloride 10% (styptic lint).

**Sponges, Carbolised,** have fallen into disuse but some surgeons still prefer them to cotton swabs. They are available thin and flat and can be kept in 1 in 20 phenol solution.

Sponge is the cleaned skeleton of a marine animal, *Spongia officinalis*.

**Spongio-Piline.** Thick felt with waterproof india-rubber backing for applying warm moist dressings.

**Impermeable Piline.** One-third the thickness of spongio-piline of felt, and instead of the waterproof india-rubber backing of the former, there is an antiseptic material, not affected by heat or strong spirit. For applying liniments in rheumatism, and where warmth is desired simultaneously.

**Stupa (B.P.C.).** TOW. *Syn.* UNMEDICATED TOW.

Jute fibre of good average quality in cheese rolls.

**Tela Carbasi et Gossypii (B.P.C.).** GAUZE AND COTTON TISSUE. *Syn.* ABSORBENT GAUZE TISSUE.

Consists of a thick layer of absorbent cotton wool enclosed in tubular absorbent gauze. It is also prepared medicated with boric acid, trinitrophenol, iodoform, [P2] mercuric iodide, [P1] mercury and zinc cyanide, [P2] phenol or thymol.

**Eye Pads** are ready cut, round or oval, consisting of a layer of wool between two sheets of gauze.

**Tela Carbasi et Ligni (B.P.C.).** CELLULOSE TISSUE. *Syn.* GAUZE AND CELLULOSE WADDING TISSUE.

Consists of a thick layer of cellulose wadding enclosed in tubular absorbent gauze.

**Dental Dressings.**

For dental use are prepared:—

**Aseptic Dental Napkins.**

**Absorbent Dental Rolls.** As a substitute for the napkin or rubber dam. For covering the mouths of the salivary ducts, a section may be placed on either side of a tooth, or the entire roll may be bent round the outside of the arch or under the tongue. No. 1, diameter  $\frac{3}{8}$  inch; No. 2,  $\frac{1}{2}$  inch; No. 3,  $\frac{3}{4}$  inch; No. 4,  $\frac{1}{2}$  inch; in  $1\frac{1}{2}$  or 6 inch lengths.

**Non-absorbent Dental Rolls.** To replace the rubber dam. In crown and bridge work. May be used in connection with the saliva ejector.

**Sterilised Absorbent Pledgets** for wiping out cavities.

**Aseptic Absorbent Points** are prepared for drying pulp canals.

**Sterilised Bibulous Paper**, in sheets, 3 inches by 10 inches.

**Carbonised Cotton** for filling pulp canals, and for treatment of exposed pulps.

**Sphagnum.** *Syn.* TURF MOSS, BOG MOSS. The dried moss, numerous varieties of which are indigenous to Gt. Britain. Is used as an absorbent dressing and for other purposes where absorbency is required. It has the advantage that the absorbed liquid does not merely wet the surface but is absorbed into the cells of the moss which therefore does not feel wet. The plant in its dry condition will absorb upwards of 20 times its weight of water or discharge. For taking up urinary discharge in bladder, kidney and dropsical affections the material is pre-eminently suitable. The dressing is also useful as a bedding for insane persons.

**Cavendish Moss Sheets** (*Martindale, London*) are sheets of compressed sphagnum, 24 by 15 inches by  $\frac{1}{4}$  inch approximately in thickness. Gauze-covered moss, loose moss dressings, moss pillows and [P2] sublimated moss (0.25% of mercuric chloride) are also available.

**Laminaria Digitata.** *Syn.* SEA TANGLE. From this seaweed "laminaria tents" are made for gynecological and surgical use. Placed in contact with moisture they swell to three times their original size in dry state. The laminaria is sterilised by drying after immersion in acetone, chloroform or alcohol 90% under pressure at 133°, or by placing in saturated solution of iodoform in ether or in sublimate solution.

**Stipes Laminariæ** (*P. Helv. V*) is from *L. hyperborea* and consists of the pseudo petiole. *P. Dan.* admits both *L. digitata* and *L. hyperborea*.

## HAMAMELIS

**Hamamelidis Cortex** (*B.P.C.*), *syn.* WITCH HAZEL BARK, is the bark of *Hamamelis virginiana* (*Hamamelidaceæ*), and contains about 6% of tannin. It is imported from the United States.

**Uses.** A local astringent and hæmostatic.

**Tinctura Hamamelidis** (*B.P.C.*).

**Dose.**— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.). 1 in 10 of alcôhol 45%.

$\frac{1}{2}$  drachm of the tincture in 1 ounce of cold water may be given as a retention enema for bleeding piles every day.

A lotion of 1 or 2 dr. with water to 1 oz. is a useful application to bruises and small wounds.

**Hamamelis** (*B.P., P. Helv. V, Fr. Cx.*). *Syn.* HAMAMELIDIS FOLIA, WITCH HAZEL LEAVES.

Consists of the dried leaves of *Hamamelis virginiana*.

**Uses.** Employed in the form of a liquid extract as a local application to sprains, bruises, superficial wounds and epistaxis; also as a gargle in sore throat and hoarseness, and in the form of suppositories for internal hæmorrhoids and ointment for external hæmorrhoids.

**Extractum Hamamelidis (B.P.C.).** *Syn.* HAMAMELIN, HAMAMELIDIN. *Dose.*—1 to 5 grains (0.06 to 0.3 g.) in pill.

A dry alcoholic extract from the leaf. It may be brown or green in colour according to the leaf from which it is prepared and the temperature of evaporation.

It was suggested (H. Berry, *Pharm. J.*, ii/1936, 247) that alcohol 45% should be used in the preparation of dry extract of hamamelis, since such an extract has the advantages of being readily soluble in glycerin and of not varying in colour whilst retaining the full tannin content of the drug. An extract prepared on these lines has been recommended for inclusion in the *B.P.* by the Pharmacy and Pharmacognosy Committee of the Pharmacopœia Commission (*Report* 13).

A suppository of 1 to 3 grains with cacao butter is useful for piles.

**Extractum Hamamelidis Liquidum (B.P.).**

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

A 1 in 1 preparation of the dried leaves made with 45% alcohol.

**Liquor Hamamelidis (B.P.C.).** *Syn.* DISTILLED WITCH HAZEL. *Dose.*— $\frac{1}{2}$  to 3 drachms (2 to 12 ml.). 1 in 1, prepared by distillation from the fresh leaves or twigs. Used externally for piles, and by rectal injection for internal piles, to check epistaxis and bleeding from tooth sockets, also for application to bruises.

For piles, 5 minims of a mixture of equal parts of the liquor and glycerin containing 10% of phenol, have been injected into the piles hypodermically.

**Pasta Hamamelidis (B.P.C.).** *Syn.* WITCH HAZEL CREAM.

A non-greasy stearate cream containing about 50% *w/w* of solution of hamamelis. Useful basis for medicated creams.

**Cremer Hamamelidis (L.H.).** Solution of hamamelis 60 m., yellow soft paraffin 120 gr., wool fat to 1 oz.

**Hazel Foam (Martindale, London).** A soothing, non-greasy ointment basis. May be medicated with all forms of antiseptics and skin applications, *e.g.*, ichthammol 3%; ichthammol 3 to 10% with resorcin 5%; salicylic acid 1%; cade oil 5%; phenol 1 to 2½%; solution of coal tar 10%.

**Suppositorium Hamamelini et Zinci Oxidi (B.P.C.)** contains 3 gr. of extract of hamamelis and 10 gr. of zinc oxide with oil of theobroma to 30 gr.

[D-P1-S1] **Compound Hamamelis Suppository.** Hamamelin 1 gr., or caïne 5 gr., cocaine hydrochloride  $\frac{1}{2}$  gr., extract of opium  $\frac{1}{2}$  gr., extract of be donna  $\frac{1}{2}$  gr., oil of theobroma to 60 gr. For internal hæmorrhoids.

[P1-S1] **Suppositorium Hamamelini, Conii et Eucainæ.**

Hamamelin 5 gr., extract of conium 4 gr., benzamine  $\frac{1}{2}$  gr. in glycerin suppository mass to 30 gr. Rub down the drugs first with a very little warm water. In painful hæmorrhoids.

[D-P1-S1] **Suppositorium Hamamelini et Hydrargyri Compositum.**

Mercurial ointment 1 gr., hamamelin 2 gr., extract of ergot 1 gr., extract of belladonna  $\frac{1}{2}$  gr., morphine sulphate  $\frac{1}{2}$  gr., tragacanth *q.s.*, oil of theobroma to 15 gr.

The mercury to act on prostatic hyperæmia often present with piles, hamamelin on the mucous membrane, ergot on the muscular walls of blood vessels, belladonna the same and sedative, morphine analgesic and vasoconstrictor. The theobroma oil as local mechanical lubricant and the tragacanth for consistency.

**Unguentum Hamamelidis (B.P.C.).** Contains 10% of the liquid extract. It is largely employed for piles. It may be filled into hollow suppositories. A combination [D-P1-81] with cocaine 2% is useful.

[P1] **Hæmorrhæline (Hewlett, London).** An ointment for hæmorrhoids containing lead acetate, witch hazel, morphine and lanolin.

**Ficaria (B.P.C.).** *Syn.* PILEWORT, LESSER CELANDINE. The fresh herb *Ranunculus Ficaria* (Ranunculaceæ). An old remedy for hæmorrhoids.

**Unguentum Ficarise (B.P.C.)** is prepared by digesting the herb in benzoated lard. Suppositories are also prepared from a mass made by melting together 4 parts of ointment and 1 part of spermaceti.

**Lawsonia (B.P.C.).** *Syn.* HENNA. The powdered leaf of *L. alba* (Lythraceæ). It is employed as a hair dye. In some cases cupric chloride and pyrogallol are used in conjunction with henna, and again borax is occasionally used as an adjuvant, the idea being no doubt that the pyrogallol oxidises more readily in alkaline solution. The quantities relative to the henna in such cases are exceedingly small.

**Sambucus (B.P.C., Fr. Cx., P. Helv. V, P. Dan.).** *Syn.* ELDER FLOWERS. The fresh or dried corollas and stamens of *S. nigra* (Caprifoliaceæ). An infusion is a domestic remedy for bruises, etc., also a pomade prepared by digesting the flowers in melted lard.

**Sambuci Folium** was formerly used for the preparation of **Unguentum Sambuci Viride** by digestion in lard and also of **Oleum Sambuci Viride** by digesting 1 of bruised fresh leaves in 3 of linseed oil.

**Aqua Sambuci (B.P.C.).** Triple elder-flower water diluted, immediately before use, with twice its volume of distilled water.

**Aqua Sambuci Triplex (B.P.C.).** The undiluted elder-flower water of commerce consisting of a saturated solution of the oil.

**Unguentum Sambuci (B.P.C.).** Triple elder-flower water 20% in simple ointment, coloured with chlorophyll.

## HEPAR

(LIVER EXTRACTS, AND STOMACH PRODUCTS.)

The use of liver in the treatment of pernicious anæmia was founded on the observation (Whipple and co-workers, *Amer. J. Physiol.*, 1920, 53, 36) that the administration of liver to dogs which had been subjected to a hæmorrhage markedly accelerated the regeneration of blood. Successful experiments on human subjects with pernicious anæmia were described first by Minot and Murphy (*J. Amer. med. Ass.*, ii/1926, 470). The diet advocated included about  $\frac{1}{2}$  lb. of cooked liver daily and was rich in proteins, iron, vegetables and fruit, and poor in fat. These results were confirmed and extended by Minot and Murphy (*Brit. med. J.*, ii/1927, 674), and others. The liver may be given either cooked



or raw. In the former case it may be cooked by any convenient method, but must not be subjected to prolonged boiling. Raw liver may be cut up into pieces and taken in cachets.

Following confirmation of the value of liver in the treatment of pernicious anæmia attempts were made to produce active extracts so as to avoid the difficulty of taking the large quantity necessary and also the tendency to produce nausea. Beginning with the work of Cohn (*J. Biol. Chem.*, 1927, 74, 69), who prepared an active extract known as "Fraction G," successive investigations have resulted in the production of extracts of increasing potencies.

For further details of early work on liver treatment see G. R. Minot's Nobel Lecture, "The Development of Liver Therapy in Pernicious Anæmia," *Lancet*, i/1935, 361.

### **Extractum Hepatis Siccum (B.P.).**

**Dose.**—The quantity equivalent to about  $\frac{1}{2}$  lb. (225 g.) of fresh liver.

It is difficult, if not criminal, to lay down any hard-and-fast rules concerning dosage. Response in different people is extremely variable. Orally, some patients require extract made from 3 lbs. of liver a day while others respond satisfactorily to a similar extract from  $\frac{1}{2}$  lb. of liver and there is the same variability in response to parenteral administration. Moreover, extracts vary enormously in potency—even with two batches of extract prepared by the same process one may be active and the other not, and an extract made from 6 g. of liver may be more potent than one made from 100 g.—Janet Vaughan, *Lancet*, ii/1933, 64.

A selected fraction of an alcoholic extract of ox or sheep liver containing the specific principle active in pernicious anæmia. It contains not less than one-eleventh its weight of sodium chloride and occurs as a light brown hygroscopic powder with a meat-like odour and taste. A method of preparation, originally published by the Medical Research Council, is described in the B.P. See also J. B. Collip, *Canad. med. Ass. J.*, i/1928, 392.

In order to free liver extract of impurities, a paste of the water-soluble constituents of liver is mixed with 60 to 80% alcohol and cooled to not over  $-15^{\circ}\text{F.}$ , at which temperature it is maintained sufficiently long to ensure complete precipitation of substances insoluble at this temperature. The precipitate is then separated from the alcoholic solution.—H. L. Keil, per *J. Amer. pharm. Ass., pharm. Abstr.*, 1939, 345.

**Home-made Liver Extract.** Extract 10 oz. of minced beef liver with cold water. Precipitate inert proteins by boiling and strain off. The clear yellow liquid obtained equals in activity the original amount of liver when ingested. Volume of liquid should be about 18 oz.—*Pharm. J.*, ii/1931, 50.

**Uses.** The administration of liver or of liver extract to pernicious anæmia patients produces a rise in the red blood cell count and a slower improvement in spinal cord symptoms. The furred tongue and diarrhoea disappear, but gastric acidity does not return and the administration of hydrochloric acid should be continued. The general health and strength of the patient return to normal except for severe cord symptoms. The reticulocytes, which are usually less than 2% before treatment, show an increase by the fourth day after commencing liver therapy and reach a peak between the seventh and tenth days; the height of the peak is inversely proportional to the initial red cell count. From an initial red cell count of 1 million a reticulocyte peak of 40% may

follow; from 2 million red cells the peak may be 20%, but initial red cell counts of over  $3\frac{1}{2}$  million do not show any rise in reticulocytes. Within 3 weeks after the commencement of the treatment the reticulocyte count falls to normal level. A rise in hæmoglobin and red blood cell count usually occurs shortly after the reticulocyte peak and approximately normal values are obtained in 1 to 2 months.

Rest in bed is essential in all cases until the red cell count has reached 4 millions and the hæmoglobin 60 to 70%.

It is important to observe that liver therapy is of no value in hypochromic anæmias, chlorosis, and anæmias due to chronic hæmorrhage, all of which respond best to iron therapy.

*Classification of the anæmias.* So far, two prominent classifications have been offered. The first is that suggested by Janet Vaughan, who states that there are three essentially different mechanisms to which anæmia may be due. These are: (1) failure or abnormality in blood production (dys hæmopoietic anæmias); (2) abnormal loss of blood (post-hæmorrhagic anæmias); (3) excessive destruction of blood (hæmolytic anæmias). The second is that of Ottenburg, who divides anæmias into three ætiological groups: (1) deficiencies; (2) injury to blood-forming organs; (3) disintegration of blood. Another suggested classification groups the anæmias in terms of the erythrocytes and the hæmoglobin content: (1) hyperchromic macrocytic anæmias (pernicious anæmia and its allies); (2) normocytic anæmias (due to excessive hæmorrhage); (3) hypochromic microcytic anæmias (covering conditions of chronic hæmorrhage as well as chlorosis and nutritional forms).—*Prescriber*, 1939, 46.

**Extractum Hepatis (U.S.P. XI).** The dried soluble fraction of mammalian livers. It must be approved by the U.S.P. Anti-anæmia Preparations Advisory Board; clinical data must be supplied of cases of treatment of Addisonian pernicious anæmia and this data must show satisfactory results when the preparation was given in the dose stated on the label.

### **Extractum Hepatis Liquidum (B.P.).**

*Dose.*—1 fl. oz. (30 ml.), equivalent to about  $\frac{1}{2}$  lb. (225 g.) of fresh liver.

The extract obtained as described for Ext. Hepatis Siccum in the B.P. is dissolved in a menstruum such that the product contains per litre the equivalent of 8000 g. of the original liver, not less than 10% *v/v* of alcohol 95% and not less than 20% *v/v* of glycerin.

### **Liquor Hepatis (U.S.P. XI).**

Like the dry extract, it must be approved by the U.S.P. Anti-anæmia Preparations Advisory Board.

**Fish Liver Extract.** An extract made from whiting, haddock and cod livers has been shown to be of remarkable potency in the treatment of pernicious anæmia, the red cell count and hæmoglobin percentage being doubled or trebled within a few days. Whiting-liver extract is more pleasant to take than that from haddock or cod, and is similar to but nicer than mammalian liver extract. The daily dose during the acute stage is the extract of 1000 g. of raw fish liver (= 500 g. of liver tissue).—L. S. P. Davidson, *Brit. med. J.*, ii/1932, 347.

### **Standardisation of Liver and Stomach Preparations for use in the Treatment of Pernicious Anæmia.**

A U.S.P. unit is the minimum amount, which, when given daily to a suitable patient with pernicious anæmia in relapse, will cause an adequate hæmatopoietic response. Inasmuch as material derived from about thirty times as much liver must be given by mouth to produce the same response as when given by injection, it has been necessary to define the "unit" either as an oral unit or as an "injectable" unit. For the purpose of standardisation the material is given daily with proper hæmatopoietic checks to at least three patients whose red blood cell counts are taken before treatment, on the day treatment is started and on the

seventh and fourteenth day of treatment. The ideal test patient should have a red blood cell count between 1 and 2.5 million per cu.mm., and should not have received antianæmic medication or blood transfusion during the previous month. Infection, marked neurological involvement, extensive arteriosclerosis, severe diarrhoea, vomiting or marked gastro-intestinal complications are factors which must be taken into account in evaluating the response. During the complete period of the "reticulocyte response" daily reticulocyte counts are made. These data are submitted to the Anti-anæmia Preparations Advisory Board of the U.S.P., which evaluates them and assigns unitage. In assigning unitage the following points are also considered:—(1) The character and degree of the reticulocyte response; (2) the rate of increase of red blood cells; (3) clinical factors modifying these responses; (4) efficiency of the method of manufacture in preserving the potency of the product; (5) the following figures:—

Initial Red Blood Cell Count (Millions per Cu.Mm.)	Peak of Reticulocyte Curve (per cent.)
1.0	41.8
1.5	28.4
2.0	18.6
2.5	11.1
3.0	5.1

These figures are not to be considered as "standards" inasmuch as modifying factors, in each individual patient, may change the interpretation of the type and degree of the response.—N.N.R., 1940, 320. See also G. R. Minot and W. B. Castle, *Lancet*, ii/1935, 319.

**Liver Extracts for Parenteral Administration.** In a small percentage of cases oral administration of liver or of extracts of liver fails to produce a reticulocyte response, possibly due to the wall of the intestine being abnormally impermeable to the active principle. Attempts were therefore made to administer liver extracts by injection. The early extracts were unsuitable for administration in this way owing to the presence of too much protein and of a principle which caused a fall in blood-pressure and which it was not found possible to remove to a sufficient extent. In 1931, W. B. Castle and F. H. L. Taylor (*J. Amer. med. Ass.*, i/1931, 1198; *Lancet*, i/1931, 857) further purified Cohn's Fraction G (p. 567), obtaining a preparation active when given intravenously. To avoid the objections to intravenous administration, a further preparation was obtained (M. B. Strauss, F. H. L. Taylor and W. B. Castle, *J. Amer. med. Ass.*, ii/1931, 313) of which 2 ml., equivalent to 10 g. of liver, was given daily by intramuscular injection. In general, extracts for parenteral administration are prepared from an aqueous extract of fresh minced liver by precipitation of proteins and other extraneous matter by means of heat and fractional precipitation with alcohol. Finally the active fraction is precipitated by alcohol 95% and may be dissolved in water and the solution sterilised, an antiseptic being usually added.

**Liquor Hepatis Purificatus (U.S.P. XI)** is the liquid extract or solution prepared for injection; it must be sterile and may contain not more than 0.5% of cresol or phenol.

There is no doubt at all that for the treatment of pernicious anæmia the use of fresh liver or oral liver extracts does not give as good results as stomach preparations or parenteral liver extracts. Extracts for intravenous injection should only be used which have been guaranteed by the manufacturers to have been clinically tested and found active in the treatment of pernicious anæmia.—J. F. Wilkinson, *Practitioner*, ii/1933, 412.

It is possible to state without hesitation that intramuscular treatment (as opposed to oral treatment) given at intervals of 2 or 3 weeks, is the cheapest and best method for maintaining a normal blood level in pernicious anæmia.—S. Davidson, *Med. Annu.*, 1935, 19.

**Suggested treatment for an average case.** In cases with a red blood cell count of 1,500,000 to 2,200,000 per cu. mm., and a hæmoglobin content of 30 to 45%, commence treatment by an intramuscular injection of 5 ml. and repeat this dose on the next day; then, on alternate days give 5, 5, 2, 2, 2, 2 ml. intramuscularly up to the end of the first fortnight. If there is a good reticulocyte response and the red cells show a satisfactory rise continue with one or two injections a week of 5 ml. intramuscularly until the blood count is normal. This treatment may be combined with the oral administration of liver, liver extract, or stomach extract, when the doses given intramuscularly may be reduced proportionately.

In very severe cases with collapse, and with a red blood cell count of 900,000 per cu. mm. and hæmoglobin content of 18%, an injection of a potent liver extract is given, preferably by intravenous injection, or 6 to 10 ml. intramuscularly. If this fails to bring about a reticulocyte response within 48 hours and shock is considered to be threatening life a blood transfusion must be given, and following this intramuscular injections of 5 ml. of liver extract daily until a satisfactory response to treatment results.

No case should be regarded as satisfactory unless the red cell count can be maintained at 5 million and the hæmoglobin at 90%. Stomach extract is the best oral preparation for maintenance purposes (from 4 to 5 oz. weekly); alternatively, from 5 to 10 ml. of liver extract intramuscularly (2 ml. = 1 lb. of liver) on two consecutive days from eight to twelve times a year.—Whitla, 8th Edn., 1938.

The dosage of injectable liver extracts should be thought of in terms of raw liver orally. The injectable preparation is 20 to 40 times more effective than the oral, hence 1 ml. of extract derived from 5 g. of raw liver actually represents 100 to 200 g. of raw liver. It is a safer plan to use a ratio of 20 in calculating the dosage.—E. A. Sharp, *J. trop. Med. (Hyg.)*, 1936, 53 and 65.

## REFERENCES TO THERAPEUTIC USES OF LIVER EXTRACTS, ORAL AND PARENTERAL

For earlier references to treatment of pernicious anæmia with liver see 20th Edn. pp. 951 and 952.

**AGRANULOCYTIC ANGINA.** Treatment by liver extract orally and parenterally; remissions occurred in five cases.—Foran-Sheaff and Trimmer, *J. Amer. med. Ass.*, i/1933, 1917.

**DISSEMINATED SCLEROSIS** treated by liver, lightly cooked,  $\frac{1}{2}$  lb. daily, with remarkable results. Method evolved in the hope that the nervous system might benefit, on the lines of pernicious anæmia.—A. Goodall and J. K. Slater, *Brit. med. J.*, i/1931, 789.

**SPRUE.** Intravenous injection of liver extract in doses equivalent to 50 g. of liver daily effective in the treatment of sprue.—Rhoads and Miller, *J. Amer. med. Ass.*, ii/1934, 387.

In London, at least 90% of patients with tropical sprue get completely well on combined liver extract *per os*,  $1\frac{1}{2}$  lbs. (700 g.) daily, and graded high protein, low fat, and low carbohydrate diet, in the ratio 1.0 to 0.3 to 1.3, respectively commencing with 500 calories and working up to 3000.—N. Hamilton Fairley, *Proc. Mayo Clin.*, 1936, 190.

**SUBACUTE COMBINED DEGENERATION.** Complete arrest of the neural lesions occurred in 26 patients with advanced subacute combined degeneration of the spinal cord treated with liver extract by intramuscular injection for a period of thirty-four months (average). By appropriate treatment with parenteral liver extract the spinal cord lesions can be prevented from developing or, if present, may be completely cured.—M. B. Strauss and associates, *J. Amer. med. Ass.*, i/1935, 1587.

The most important point in treating patients with spinal cord involvement is the maintenance of the blood at or above normal level, for even with the red blood counts as high as 4 millions the development of cord lesions has been observed, while with red cells at 5 millions or higher this has not taken place.—B. M. Fried, *J. Amer. med. Ass.*, i/1929, 1260.

The point of view which has been advanced that while nerve lesions may improve, spinal cord lesions do not, is hardly in keeping with the disappearance

of the Babinski reflex and ataxia. The rate of improvement in spinal cord symptoms is inversely proportional to their duration, the outlook for complete recovery being much brighter if symptoms have been present only for a few months; but even those of years' duration may show improvement with prolonged intensive treatment.—R. West, *J. Amer. med. Ass.*, ii/1935, 432.

**THROMBOPENIC PURPURA** of moderately severe grade with oozing from gums and ecchymoses rapidly yielded to liver treatment.—F. H. Jacob, *Brit. med. J.*, i/1931, 33.

### PROPRIETARY LIVER PREPARATIONS

**Anabolin Solution** (*Endocrines-Spicer, Watford*). Standardised extract of hepatic parenchyma free from protein and histamine, for reducing blood pressure due to toxæmia. 1 ml. reduces the arterial tension of a 10 kg. dog by 12 mm. *Dose*.—1 ml. intramuscularly every day or as found necessary. Also in tablets for oral administration, one tablet being equivalent to 1 ml. of solution. *Dose*.—1 tablet three times daily or as required.

**Anti-Menorrhagic Factor Glanules** (*Armour, London*). A non-saponifiable fraction of mammalian liver tissue, having the property of checking functional uterine hæmorrhage at any age. *Dose*.—2 capsules, three times a day during menstruation, or 1 capsule three times a day in the inter-menstrual period.

**Binsemon Tablets** (*Organon Laboratories, London*). A concentrated liver and hog's stomach preparation, tested clinically on cases of pernicious anæmia, in 0.3 g. tablets. Relapsed cases require 8 tablets daily, 4 tablets daily being the average maintenance dose.

**Bioglan 'R'** (*Bioglan Laboratories, Hertford*). Extract of calf's liver for injection, each 2 ml. ampoule containing the clinical equivalent of 80 g. of fresh liver.

**Bioglan 'R' Forte** (*Bioglan Laboratories, Hertford*). One 2 ml. ampoule contains 200 mg. of purified liver fraction. If the initial r.b.c. is above 2,000,000 one ampoule should be given at intervals of 3 weeks; if below 2,000,000, treatment should commence with an injection every week for 3 weeks, then every third week.

**Campolon** (*Bayer Products, London*). Liver extract for intramuscular injection. 2 ml. = 500 g. of liver *per os*. **Campoferron** is a form of Campolon containing 0.1% of iron and 0.003% of copper, suitable for oral administration. *Dose*.—1 to 2 teaspoonfuls three times daily.

**Cofron** (*Abbott Laboratories, London*). Each capsule represents approximately fresh liver 10 g., iron 7 mg., copper 0.27 mg. *Dose*.—3 to 5 daily. Also supplied as **Cofron Elixir**; average daily dose—6 drachms.

**Elixir Feramin** (*Duncan, Flockhart, Edinburgh*). Each fl. oz. contains the antianæmic principles of 4 oz. of fresh liver, in combination with vitamin B and iron and ammonium citrate. *Dose*.—2 tablespoonfuls twice daily. In secondary anæmia.

**Erythgen Liver Extract** (*Carmick, Newark, N.J.; Brooks & Warburton, London*). Each oz. is equivalent to 5 oz. of fresh liver. Also supplied for intramuscular injection (2.5 ml. equivalent to 600 g. of fresh liver).

**Examen** (*Glaxo Laboratories, London*). Liver extract for injection, containing in 2 ml. 10 to 15 mg. of solids equivalent to 100 g. of liver. *Dose*.—Initially 4 ml., then 2 ml. fortnightly until the blood count is normal. Maintenance dose, 2 ml. every 3 to 5 weeks; by intramuscular injection.

**Exhepa** (*Bencard, London*). Brand of dried liver extract.

**Fercupar** (*Richter, London*). Tablets each containing dry extract of liver  $2\frac{1}{2}$  gr., ferrous chloride 1 gr., copper sulphate  $\frac{1}{32}$  gr. *Dose*.—2 thrice daily.

**Ferroglandoid** (*Armour, London*). A concentrated fluid extract of liver containing 12 gr. of iron and ammonium citrate in each drachm. *Dose*.—1 to 2 teaspoonfuls three times daily. In pernicious and secondary anæmias and as a general tonic.

**Ferroglandoid Glanules** (*Armour, London*). 10 m. capsules containing 0.1152 g. of liver concentrate (1:125), 0.2 g. of iron and ammonium citrate, 0.02 g. of vitamin B adsorbate (standardised to contain 300 i.u. per g. of vitamin B), and 75 Sherman-Borquin units per g. of vitamin B<sub>12</sub>, 0.2064 g. of vegetable oil. *Dose*.—1 to 3 capsules three times daily. In pernicious and secondary anæmias and as a general tonic.

**Hæmatinic Compound** (*John Wyeth, London*). One "Plastule" contains the equivalent of 210 gr. of fresh liver, with exsiccated ferrous sulphate 10 gr., and dried yeast 3 gr.

**Hæmex** (*Paines & Byrne, London*). A purified liver fraction solution. *Dose*.—From 2 to 4 ml. weekly by injection. Pernicious anæmia.

**Hæmochromin** (*G. W. Carnick, Newark, N.J.; Brooks & Warburton, London*). Each tablet contains  $2\frac{1}{2}$  grains of liver extract and the equivalent of  $2\frac{1}{2}$  grains of ferrous sulphate (U.S.P.). *Dose*.—1 to 2 thrice daily after meals.

**Hebula Capsules** (*Squibb, New York; Savory & Moore, London*). Contain liver extract from 16 g. of fresh liver, exsiccated ferrous sulphate 2 gr., vitamin B<sub>1</sub> 25 i.u., and vitamin B complex. Secondary anæmia, nutritional anæmia, and general debility.

**Hepa Simplex** (*Bencard, London*). Liver extract in powder form. Also supplied containing 1% of iron.

**Hepamult** (*Norgine, London*). Standardised liver extract in palatable granular form (10 g. = 8 oz. of fresh liver). *Dose*.—10 to 20 g. daily. **Ferro-Hepamult** is Hepamult with 1.7 g. of iron in 10 g.

**Heparmone** (*Lilly, London*). A sterile refined solution prepared from liver for the treatment of eclampsia. *Dose*.—10 ml. or more intramuscularly (or intravenously in emergency).

**Hepastab** (*Boots, Nottingham*). Liver extract for intramuscular injection. *Dose*.—2 ml. daily for 3 or 4 days; maintenance dose, 2 ml. at intervals of 2 to 6 weeks. **Hepastab No. 2** is a specially purified form. *Dose*.—2 ml. intramuscularly or intravenously.

**Hepatex Oral** (*Evans, Sons, Lescher & Webb, Liverpool*). A liquid extract. *Dose*.—1 dr. = 2 oz. fresh liver. Also supplied with iron (1 gr. per drachm). **Hepatex P.A.F.** is a purified and potent extract (5 ml. = 100 g. of fresh liver) given intravenously. Practically free from protein and does not affect blood pressure. *Dose*.—5 ml. undiluted injected in 2 to  $2\frac{1}{2}$  minutes, either per week or per day, according to severity of case. **Neo-Hepatex** is a potent extract for intramuscular injection. *Dose*.—In mild cases, 1 to 2 ml. on each of 3 successive days, then 2 ml. at 7 to 10 day intervals; in severe cases, 4 ml. [P1-81] **Hepatex Compound Intramuscular** (H.C.I.) contains in 1 ml. Neo-Hepatex 0.8 ml., soluble iron arsenite 0.03 g., strychnine nitrate 0.0005 g., sodium glycerophosphate 0.045 g. *Dose*.—1 to 2 ml. daily.

**Hepatex—T (Tropical)** (*Evans, Sons, Lescher & Webb, Liverpool*). A solution of the principles of mammalian liver including vitamin B<sub>1</sub> and vitamin B<sub>2</sub> complex effective in the treatment of nutritional macrocytic anæmia. Administered by intramuscular injection, the initial dose being 2 ml. and subsequent doses varied as required.

**Hepol** (*Allen & Hanburys, London*). Concentrated liver extract. Issued in both dry and liquid forms for oral use, and as elixir and capsules; also in ampoules for intramuscular and intravenous injection. **Ana-Hepol** is supplied in 2 ml. ampoules for injection.

**Hepovite** (*Evans, Sons, Lescher & Webb, Liverpool*). A preparation of Hepatex, with vitamin C, hæmoglobin and iron. *Dose*.—One tablespoonful twice daily. In secondary anæmia, debility and neurasthenia.

**Heprona** (*Evans, Sons, Lescher & Webb, Liverpool*). Preparation containing "Hepatex" liver extract, iron, sodium glycerophosphate and vitamins B<sub>1</sub>, B<sub>2</sub>, and C with traces of copper. For use as a tonic in secondary anæmias and convalescence. *Dose*.—2 to 4 drachms once or twice daily; for children, half this quantity.

**Ivestron** (*Wyleys, Coventry*). Compound liver extract containing the therapeutic principles of fresh liver and yeast, with iron, manganese and red bone marrow. *Dose*.—2 to 4 fl. dr. twice daily.

**Jectemia** (*Sharp & Dohme, London*). Liquid liver extract for intramuscular injection. 1 ml. contains the antianæmic principle derived from 100 g. of fresh calves' liver. *Dose*.—2 ml. repeated weekly until a normal blood count is attained. Pernicious anæmia.

**Lextron** (*Lilly, London*). Capsules contain liver-stomach concentrate 7 gr., green iron and ammonium citrate 3 gr. with vitamins B<sub>1</sub> and B<sub>2</sub>, 20 Sherman units of each. *Dose*.—3 or more capsules thrice daily (9 capsules produce 75% as much hæmoglobin as 300 g. of fresh liver).

**Lirimin** (*Sharp & Dohme, London*). Capsules containing concentrated liver extract 0.24 g., excised ferrous sulphate 0.3 g., vitamin B<sub>1</sub> 0.167 mg. (= 55 i.u.), vitamin B<sub>2</sub> 25 microgrammes, together with other natural factors of the vitamin B complex derived from liver. *Dose*.—1 or more capsules three times daily. Pernicious and secondary anæmias.

**Livadex** (*British Drug Houses, London*). Contains the whole of the hæmopoietic principles of fresh liver and conforms with the specifications for liquid extract of liver B.P., one fluid ounce possessing the antianæmic activity of half a pound of fresh liver.

**Liver Extract Fraction A5** (*Sharpe & Dohme, London*). A dry liver extract of which 1 g. = 20 g. of fresh liver. Also available in capsules (0.5 g.) and as a liquid (1 oz. = 8 oz. of fresh liver).

**Liveroid** (*Oxo, London*). Liquid extract of liver.

**Livogen** (*British Drug Houses, London*). Liquid liver extract, hæmoglobin and vitamin B. A tonic in all anæmic conditions.

**Livron** (*Boots, Nottingham*). Compound extract of liver, malt, iron and yeast (1 oz. contains 90 gr. of iron and ammonium citrate). *Dose*.—1 tablespoonful twice daily. In secondary anæmias and as a general tonic.

**Neobovinine 20** (*John Wyeth, London*). Organic compound of liver extract and beef blood. 1 fl. oz. contains 128 m. of liver extract and 2½ gr. of iron. *Dose*.—1 tablespoonful four times daily. Reconstructive tonic.

**Parenamps** (*Paines & Byrne, London*). Liver extract for intramuscular injection, 2 ml. = clinical equivalent of 5000 g. of fresh liver given orally.

**Perhepar** (*Richter, London*). Liver extract. 1 g. or 10 ml. = 100 g. of fresh liver. Supplied in tablets and ampoules.

**Pernæmon Forte** (*Organon Laboratories, London*). An aqueous concentrated solution of liver extract. *Dose*.—4 ml. on the first day, repeated in 3 or 4 weeks. By intramuscular injection. Subsequent treatment is varied to suit the patient. **Pernæmon Simplex** is a similar preparation but only one-fifth as potent.

**Proethron** (*Armour, London*). Sterile isotonic liver extract for intramuscular injection. *Dose*.—2 to 4 ml. as required. 2 ml. given daily for 3 to 4 days will produce maximum reticulocyte response in some cases. If cord lesions are present 4 ml. should be given daily for a protracted period, the dose being gradually reduced to the minimum which will prevent progression of neural symptoms. A monthly depot dosage of 2 to 4 ml. is often adequate.

**Proethron Forte** (*Armour, London*). A liver extract for intramuscular injection, each ml. representing the antianæmia principle from 100 g. of calf liver. *Dose*.—Initially 2 ml., then repeat every seven days. For maintenance: ½ ml. weekly, or 1 ml. every fortnight.

**Reticulogen** (*Lilly, London*). Solution of liver extract for injection combined with vitamin B<sub>1</sub>. 0.5 ml. contains the therapeutic equivalent of 6½ to 10 lb. of fresh liver and 500 i.u. of vitamin B<sub>1</sub>. The hæmopoietic activity is standardised on cases of pernicious anæmia in relapse. Vitamin B<sub>1</sub> is included for its possible effect on the central and peripheral nervous manifestations. *Dose*.—The average initial dosage for cases in relapse is 0.5 ml. on three successive days, followed by 0.5 ml. at intervals of 1 to 2 weeks.

**Trephonyl** (*Bengué, London*). Fetal liver extract, horse serum and embryonic juice. *Dose*.—10 to 20 ml. daily *per os*. In all types of anæmia and in convalescence.

**Xorox** (*Napp, London*). Hæmotonic prepared from liver, spleen, stomach and anterior pituitary. *Dose*.—In adults, 2 tablets thrice daily; smaller doses in children. In anæmia and debility and for backward children.

### Hæmopoietic Principle in Liver.

The concentration of the active principle was carried a stage further by the work of Dakin and West (*J. biol. Chem.*, 1935, 109, 489). Starting with Cohn's "Fraction G" a yield of 1% of a highly potent product was obtained. The method adopted involved a complex series of precipitations in which, after removal of inert material with calcium acetate in alcoholic solution, the active

principle was precipitated with Reinecke salt (ammonium tetra-thiocyanatodiammino-chromium,  $\text{NH}_4[\text{Cr}(\text{NH}_3)_2(\text{SCN})_4]\cdot\text{H}_2\text{O}$ ), regenerated by means of dimethylaniline and amyl alcohol and further purified by repeated precipitation with ammonium sulphate and magnesium sulphate. To this product the name **Anahæmin** was given. It is a light buff-coloured granular powder, soluble in water and dilute alcohol, but insoluble in dehydrated alcohol and in ether. On hydrolysis it yields an aminohexose and a number of amino-acids. Pyrimidine or purine bases are absent. The substance is slowly decomposed by pepsin and more rapidly by erepsin and alkalis. Pancreatic juice has no effect upon it. 30 mg. on injection gave a perceptible reticulocyte response and 80 mg. gave a maximum response.

More recent work has led to the conclusion that the hæmopoietic principle is a combination of two factors each having a different action. Thus, Wills, Clutterbuck and Evans (*Lancet*, i/1937, 311) reported the isolation of two factors from Campolon (a fractionated liver extract for parenteral use, *q.v.*), one soluble and the other insoluble in ammonium sulphate, the former being effective against the nutritional macrocytic anæmia of monkeys, and the latter, containing the anahæmin, being inactive against this anæmia but curative of pernicious anæmia.

The results in 86 cases of pernicious anæmia indicate that anahæmin is highly active for blood regeneration. Total quantities of 1 to 6 ml. (100 to 600 mg., average amount 359 mg.) administered, usually in divided doses, to 11 cases with initial red blood cell counts below 2 millions per c.mm. were sufficient to cause an average increase of erythrocyte concentration amounting to 2.31 millions in 40 days. Good responses followed the administration of amounts sometimes as small as 10 mg. daily or 100 to 200 mg. as a single dose. For maximal reticulocyte responses and for the production of red blood cells at a maximal rate, larger doses were usually required. There is not sufficient data to assess quantitatively the potency of anahæmin as compared with other liver extracts, but no other liver extract given in the small amounts used in the investigation produced such striking results.—C. C. Ungley, L. S. P. Davidson and E. J. Wayne, *Lancet*, i/1936, 349.

The fractionation of liver extracts containing the anti-pernicious anæmia principle by means of Reinecke acid to yield a more highly potent fraction has been confirmed. Using this method products have been obtained of which 58 mg. produced a maximal reticulocyte response and a rapid remission in a patient with pernicious anæmia. Applying this method to other methods of separation a further increase in hæmopoietic potency has been secured so that as little as 18 mg. of the product has been sufficient to initiate a maximal reticulocyte response and rapid remissions in pernicious anæmia.—J. F. Wilkinson, *Lancet*, i/1936, 354.

Further purification effected by solution in 2½% *v/w* of 95% phenol and fractional precipitation with anhydrous methyl alcohol. The second fraction was obtained as a light buff-coloured powder containing 14.3% of N. By administering the materials to be compared to the same individual in consecutive periods of 10 to 14 days it was found that 2 mg. of the purified fraction was more potent than 5 mg. of the original anahæmin.—C. C. Ungley, *Lancet*, ii/1936, 1513.

Purified liver extracts (anahæmin and Examen), fully active in pernicious anæmia, were found inactive in nutritional macrocytic anæmia of monkeys. Campolon can be fractionated by saturation with ammonium sulphate into insoluble and soluble portions. The insoluble part is also highly potent in untreated pernicious anæmia but inactive in the monkey anæmia, while the soluble part is highly active in both the human and the animal conditions. The monkey anæmia is therefore due, in part at least, to lack of an unidentified



factor, and some cases of pernicious anaemia may also be due to lack of this second factor. This accounts for the occurrence of those cases of pernicious anaemia which do not respond to purified extracts such as anahæmin but readily respond to cruder extracts such as Campolon. The distribution of the new factor in products such as yeast, Marmite, wheat-germ and liver suggests a relationship with the vitamin B complex.—L. Wills *et al.*, *Biochem. J.*, 1937, 2136.

Tropical macrocytic anaemia does not respond to the more highly purified liver extracts, which contain the liver principle curative in pernicious anaemia in relatively pure form. This fact further differentiates this disease from pernicious anaemia and demonstrates the presence of a new hæmopoietic factor in crude liver and autolysed yeast extracts. This factor is almost certainly identical with the one described in the production and cure of the nutritional macrocytic anaemia of monkeys; it is not vitamin B<sub>1</sub>, B<sub>6</sub>, lactoflavin, or nicotinic acid but has not yet been separated from the yeast-filler's earth filtrate of Edgar and Macrae.—L. Wills and B. D. F. Evans, *Lancet*, ii/1938, 416.

Nutritional macrocytic anaemia responds as readily to highly purified preparations such as anahæmin as it does to the cruder liver preparations.—H. Foy and A. Kondi, *Lancet*, ii/1939, 360.

**Anahæmin B.D.H.** (*British Drug Houses, London*). The active hæmopoietic principle of liver of Dakin and West. *Dose*.—2 ml. (200 mg.) injected monthly is an adequate dose for average cases, though in severe cases up to 4 ml. may be necessary.

### Heparin.

*Dose*.—75 to 150 mg. (or 1 mg. per kilo bodyweight) intravenously in the form of a 5% saline solution.

Heparin is the anticoagulant substance prepared from liver. It has been obtained in the pure state by the crystallisation of its barium salt, and appears to be a polysulphuric ester of mucoitin, a complex of acetylglucosamine and glucuronic acid. The following formula has been proposed:— $C_{22}H_{29}O_{15}(OSO_3H)_5(COOH)_2(NH\cdot CO\cdot CH_3)_2$ . The anticoagulant effect of heparin is expressed in terms of units, of which there are a number of definitions. The Toronto unit is the activity of 0.01 mg. of the crystalline barium salt. The Howell unit is the weight of heparin required to prevent the coagulation of 1 ml. of citrated and recalcified blood plasma for four hours at 37°; the latter unit is about one-fifth of the Toronto unit.

*Uses*. It is the most active of all anticoagulants, 1 mg. per kilo bodyweight given intravenously raising the coagulation time in man by about 40 minutes. Heparin is chiefly employed in blood transfusion, the solution being injected into the vein of a donor and blood withdrawn 10 minutes later. The coagulability of the donor's blood is reduced but not that of the recipient. Transfusion should be carried out within half an hour of injection. Alternatively heparin may be added to the blood after withdrawal, 20 mg. being sufficient for 500 ml. of blood.

Heparin may also be employed in the treatment of thrombosis and post-operatively for the prevention of thrombosis.

The therapeutic possibilities of heparin.—*Lancet*, i/1938, 677.

In the treatment of patients with heparin it is sometimes desirable to restore the original coagulation-time of the blood, as for instance, when heparin has been given during an operation on blood vessels or when hæmorrhages unexpectedly set in during the course of heparin treatment. For the purpose of neutralising the action of heparin the most effective method is the intravenous injection of protamine sulphate. In general an amount of protamine sulphate

which is 50 to 70% of the amount of heparin given will neutralise it. The protamine employed is a 2% solution of clupein sulphate in dilute hydrochloric acid, pH 2.7, sterilised in an autoclave. The administration of from 50 to 150 mg. of protamine sulphate by this means seems to be practicable. The hæmostatic action of protamine administered in this way against parenchymatous hæmorrhages was much more effective than that of Stypven, but protamine injections in such case must only be used as a last resort.—E. Jorpes *et al.*, *Lancet*, ii/1939, 975.

**BLOOD TRANSFUSION.** By adding heparin to the blood after withdrawal or by injecting it into the donor before transfusion a sufficient delay in coagulation can be achieved to enable a successful transfusion to be carried out without ill effects on the donor or the recipient. The heparin is injected into the donor, the blood withdrawn after some minutes, collected in an unparaffined syringe or bottle, and injected directly into the patient.—H. Knoll and O. Schürch, *Lancet*, i/1938, 1387.

The use of heparin as an anticoagulant in blood transfusions. It may be used either by heparinising the drawn blood or by heparinising the donor by intravenous injection (1 mg. per kilo bodyweight, or about 1.5 ml. of a 5% solution). None of the 23 donors so treated suffered any ill effects, either immediate or late, and no toxic effects were observed in the patients receiving the heparinised blood.—S. W. Sappington, *J. Amer. med. Ass.*, ii/1939, 22.

**THROMBOSIS.** In a group of 315 cases treated post-operatively with heparin injections not one case of phlebitis, thrombosis or pulmonary embolism occurred. Seven cases of pulmonary embolism with infarcts arising from thrombophlebitis were also treated and there was rapid clinical improvement within 24 hours. Embolectomy was carried out successfully in four cases of embolism, the injected heparin keeping the vessels clear. The method of administration was by intravenous drip, the injection being given in a superficial vein through an ordinary steel needle left undisturbed for three to eight days. Sufficient heparin was added to the salt solution to increase the clotting time to about 15 minutes. Usually the heparin addition was in the proportion of 10 units to 1 ml. saline, i.e., on an average 25 to 30 drops per minute. The injections were continued until the state of shock had passed and blood pressure and circulation had returned to normal. Heparin should not be employed when active hæmorrhage is present and should as a rule be deferred for 4 to 24 hours after operation. Twenty-eight cases of spontaneous phlebitis responded well to the treatment. In the selection of suitable cases, the blood-clotting time, prothrombin index, platelet count, bleeding time, and ordinary blood analyses must be taken and a family or personal history of embolism should be taken into account.—G. D. W. Murray and C. H. Best, *Ann. Surg.*, 1938, 108, 163.

Thrombosis of central vein of retina successfully treated by heparin intravenously, using a 5% solution of standard potency. Three to four daily doses of heparin of 1.66 mg. per kg. bodyweight were given during a period of about 10 days without any perceptible inconveniences.—N. Holmin and K. G. Floman, *Lancet*, i/1938, 664.

Thrombosis of the posterior-inferior cerebellar artery successfully treated by intravenous injections of 5% solution, with a dose of 150 mg. three times daily.—J. H. Magnusson, *Lancet*, i/1938, 666.

**Liquemin (Roche Products, Welwyn Garden City).** Solution of heparin containing 4 mg. per ml., corresponding to 2000 anticoagulant units as defined by Reinert and Winterstein. For blood transfusion 0.5 ml. is added to each 100 ml. of blood or 15 to 30 ml. may be injected intravenously into the donor before transfusion. For delaying the blood coagulation rate in other conditions the dose is 5 to 10 ml.

### **Stomach Tissue.**

Acting on the suggestion of Castle (*Proc. R. Soc. Med.*, ii/1929, 58) that the stomach secretes a factor which reacts with meat to give a principle which is effective in pernicious anæmia, a desiccated preparation of whole stomach from the pig, freed from fat, of which 30 g. was equivalent to 218 g. of fresh stomach, was tested clinically by Sturgis and Isaacs (*J. Amer. med. Ass.*, ii/1929, 747) and found effective in doses of 15 to 30 g. daily, the activity being

equivalent to that of an active liver extract representing 300 to 600 g. of fresh liver.

**Ventriculus Desiccatus (B.P.C.).** *Syn. and Prop. Names.* DESICCATED STOMACH, ERYTHROID (Oxo, London), EUGASTROL (Allen & Hanburys, London), EXTOMAK (Benger's Food, Manchester), GASTER SICCATA (British Drug Houses, London), GASTREXO (Evans, Sons, Lescher & Webb, Liverpool), KYTOGEN (Oppenheimer, London), PEPSAC (Boots, Nottingham), VENTRAEMON (Organon Laboratories, London), VENTRICULIN (Parke, Davis, London).

*Dose.*— $\frac{1}{4}$  to 1 oz. (8 to 30 g.).

The fresh whole stomach of the pig, freed from extraneous fat, dried below 40° and ground; the dried material is defatted, dried without heat and ground to a coarse powder. Desiccated stomach should not be heated before administration to the patient.

The initial dose of desiccated stomach should not be less than 1 oz. and this dose should be maintained till the blood count has returned to normal or till the nervous symptoms have gone, when it may be reduced gradually, but it is wise to maintain a small regular dose indefinitely.

**PERNICIOUS ANÆMIA.** Desiccated hog stomach (30 g. = 190 g. of fresh tissue) and hog stomach defatted with petroleum benzine (30 g. = 218 g. fresh tissue) produce satisfactory remission. 15 to 30 g. equal in effect to 300 to 600 g. fresh liver.—E. A. Sharpe, *J. Amer. med. Ass.*, ii/1929, 749.

Undoubtedly better than liver. Erythrocytes and hæmoglobin increased 157% and 94% respectively, compared with 90% and 77% respectively with liver. Hydrochloric acid and pepsin do not appear to be necessary for relief of symptoms.—J. F. Wilkinson, *Brit. med. J.*, i/1931, 85. See also C. S. Don and C. E. Jenkins, *ibid.*, 158.

A highly potent extract is obtained by incubating Cohn's "Fraction G" with stomach tissue. 6 g. daily is a sufficient dose.—G. B. Walden and G. H. A. Clowes, *Proc. Soc. exp. Biol., N.Y.*, i/1932, 873.

Only tissue from the pyloric end of the stomach is effective.—E. Meulengracht, *Proc. R. Soc. Med.*, i/1935, 841.

The development of remedies for the treatment of pernicious anæmia—general discussion with bibliography.—W. B. Castle, *Amer. J. Pharm.*, 1936, 55.

PELLAGRA treated with desiccated stomach tissues.—T. D. Spies, *J. Amer. med. Ass.*, i/1935, 1377.

**Extralin (Lilly, London).** Liver extract which has been incubated with stomach tissue; capsules contain 0.5 g. Maintenance dose in pernicious anæmia, 3 or 4 capsules thrice daily.

**Gastrovic Leo (Bencard, London).** Desiccated hog's stomach issued in packets containing 10 g. = 100 g. of fresh stomach tissue.

**Hogastrin (Giles, Schacht, Bristol).** A liquid extract of hog stomach.

*Dose.*—1 to 2 dr.

**Hoggex (Paines & Byrne, London).** Concentrated preparations of hog stomach. Available in powder, capsules and solution. *Dose* (of powder).— $\frac{1}{4}$  to 1 oz. daily up to 2 oz. in subacute combined degeneration. Maintenance dose, about 5 g. daily. Capsules (5 g.) and solution 1 oz. are each equivalent to 80 g. of fresh stomach.

**Neo-Pepsac (Boots, Nottingham).** Concentrated fraction of hog's stomach. *Dose.*—One or more cachets daily. In pernicious anæmia.

**Perstomin (Richter, London).** Concentrated hog's stomach extract. 1 part = 24 parts of fresh substance. *Dose.*—1 teaspoonful five times daily or 1 injection of 1 ml. subcutaneously or intramuscularly daily.

**Ventron (Parke, Davis, London).** Each capsule represents 15 gr. of Ventriculin, 2 gr. of iron and sodium citrate, 20 i.u. of vitamin B<sub>12</sub> and 5 Sherman units of vitamin B<sub>12</sub>.

### The Hæmopoietic Factor in Desiccated Stomach.

Castle (*Amer. J. med. Sci.*, ii/1929, 748; *ibid.*, ii/1930, 305; *Lancet*, i/1930, 1062) showed that gastric digestion liberates anti-anæmic principles from certain foodstuffs which before digestion have no anti-anæmic properties. He regards the anti-anæmic principle as something derived from the interaction of an intrinsic factor contained in gastric juice and an extrinsic factor contained in certain foods, the product being stored in the liver. The intrinsic factor, lack of which causes Addison's anæmia, is thermolabile, being completely inactivated at 70°.

The view has been advanced that the extrinsic factor might be vitamin B<sub>12</sub>—but this is now considered unlikely since several workers have failed to produce improvement in pernicious anæmia patients by administering gastric juice with various sources of vitamin B<sub>12</sub>. It is probable that in those anæmias cured by suitable diets, the intrinsic factor is produced by the stomach, but the extrinsic factor is missing from the food, whereas in typical pernicious anæmia it is the intrinsic factor which is absent.

Pepsin is antagonistic to the anti-pernicious anæmia factor in stomach (Castle's "intrinsic factor"). His basic experiments may be explained by a mechanism which excludes the action of the so-called extrinsic factor. This is based on the demonstrated antagonism of pepsin towards the anti-pernicious anæmia factor and also on the known adsorptive capacity of protein for pepsin.—E. A. Greenspon, *J. Amer. med. Ass.*, i/1936, 270.

The above conclusions are criticised on the basis of experimental data obtained in 14 cases of pernicious anæmia. None of the findings in this investigation was incompatible with Castle's basic hypothesis.—C. C. Ungley and R. Moffett, *Lancet*, i/1936, 1233.

Hæmopoietin, the active principle in hog stomach, is much more stable than, and has different properties from, the active antianæmic principle in liver. Evidence indicates that it is of an enzyme nature and it is extremely sensitive towards heat and chemical treatment. It is present in the normal stomachs of man, carnivorous animals and omnivorous animals, but not in herbivorous animals. It is considered that the enzyme, hæmopoietin, by acting on some substance present in protein food, e.g., beef, may produce *in vivo* a substance which is stored as the active principle found in liver until it is required for red cell formation. The available evidence goes to show that true pernicious anæmia is a type of deficiency disease characterised by the absence from the gastric secretion of a specific enzyme (hæmopoietin), in addition to the pepsin and hydrochloric acid.—J. F. Wilkinson and L. Klein, *Lancet*, ii/1933, 632.

A thermo-stable hæmatopoietically active substance prepared by action of hæmopoietin on beef; similar to anti-anæmic principle of liver.—Klein and Wilkinson, *Biochem. J.*, 1934, 1584.

Addisin. A substance present in the normal gastric juice of man, destroyed by boiling, dialysable through collodion and exhaustible: withstands chemical treatment known to destroy enzymes. It has been found in the gastric juice of swine, dogs and cattle, and is believed to be widely distributed in the animal kingdom. One injection of 4 ml. of swine juice concentrated to a volume of 3 to 5%, given intramuscularly in a case of pernicious anæmia, resulted in 4 months in an increase of red blood cells from 1.6 to 4.5 millions, and of hæmoglobin from 50 to 93%. Indications are that addisin is the physiological hormone responsible for the normal state of the blood in health.—R. S. Morris and co-workers, *Brit. med. J.*, ii/1932, 1050.

**Duodeni Membranum (B.P.C.).** *Syn.* PULVIS DUODENALIS, DUODENAL POWDER. *Dose.*—3 to 10 grains (0.2 to 0.6 g.).

A greyish-brown hygroscopic powder containing one-fifth its weight of calcium phosphate. It is obtained from the upper portion of the duodenum of the pig, the mucous membrane being scraped off, scaled and powdered. It contains secretin, enterokinase, erepsin, invertase, lactase and maltase. Its

therapeutic use is based on the presence of enterokinase which produces trypsin from the trypsinogen of pancreatic juice.

#### **Liquor Duodenalis.**

A protein-free solution of the active constituents of duodenal membrane representing 10% of fresh duodenal mucous membrane. The solution is stable only if acid, sterile and stored in the dark. Has been administered by injection as a stimulant to the production of the external secretion of the pancreas, and slightly increases the secretion of bile.

**Secretin.** Extracted from the duodenal membrane with alcohol, sodium chloride or 0.4% hydrochloric acid, and nearly neutralising whilst boiling to precipitate proteins. The secretin will be left in the filtrate. It is soluble in water and alcohol. Secretin preparations are inactive *per os* since it is destroyed by pepsin and trypsin. Is usually administered as *Liquor Duodenalis*.

**Secretogen Elixir** (*G. W. Carrick, Newark, N.J.; Brooks & Warburton, London*). A preparation of secretin intended to replace pepsin and acid mixtures as indigestion remedy. It is stated to contain pyloric prosecretin (with  $\frac{1}{10}$ % of hydrochloric acid to change it to secretin) and duodenal secretin. *Dose*.—1 to 2 drachms. **Secretogen Tablets** (5 gr.) containing the duodenal and pancreatic secretins are suggested particularly in faulty digestion of starch, with fermentation and flatulence.

**Mucin.** *Dose*.—5 to 10 grains (0.3 to 0.6 g.).

This is the essential constituent of the secretions of mucous membranes (buccal, nasal, pharyngeal, etc.). It is precipitated from these by alcohol and by acetic acid. The saliva produced by the submaxillary and sublingual glands contains it, but not the parotid. It may be procured from areolar or connective tissue, and from bile.

Taken internally, *e.g.*, in tablets containing mucin 5 gr., with sodium bicarbonate 5 gr., relieves painful digestion and gastritis. Larger doses, *e.g.*, from 2 to 4 g., given at two-hourly intervals, are of value in the treatment of peptic ulcer. In the form of a spray containing mucin 5 gr., sodium bicarbonate 5 gr., menthol 1 gr., lime water  $\frac{1}{2}$  oz., distilled water  $\frac{1}{2}$  oz., has been found of value in dry catarrhs, rhinitis, etc., pharyngitis, and where incrustations are present on the laryngeal lining.

Superior to all other treatment in many throat and stomach complaints, *e.g.*, gastric ulcer. Powdered hog's stomach possibly only acts by virtue of the mucin contained.—*W. Stuart-Low, Brit. med. J.*, ii/1931, 124.

Results from gastric mucin in doses of from 90 to 100 g. daily indicate considerable promise from this form of therapy. Gastric mucin is a very viscid unpalatable preparation, and the taste is somewhat difficult to disguise.—Preliminary report of Council on Pharmacy and Chemistry, *J. Amer. med. Ass.*, i/1934, 767.

Gastric mucin has been employed in the treatment of peptic ulcers. It probably exerts a protective action by virtue of its viscous nature and of its buffer action. Symptomatic relief reported in from 63 to 93% of cases studied.—*K. A. Martin, J. Amer. med. Ass.*, i/1936, 1468.

The use of four daily doses of gastric mucin, totalling from 4 to 8 g., together with frequent feedings and the frequent administration of antispasmodics has been more successful in reducing the incidence of recurrence in peptic ulcer than any other form of management.—*C. F. G. Brown and R. E. Dolkart, J. Amer. med. Ass.*, ii/1939, 276.

**Biomucine** (*Robert et Carrière, Paris; Anglo-French Drug Co., London*). Natural mucin of the gastric mucosa, free from histamine. Supplied in cachets for treatment of hyperchlorhydria, gastric ulcer or duodenal ulcer.

**Enteromucine** (*Robert et Carrière, Paris; Anglo-French Drug Co., London*). Natural mucin of the intestinal mucosa, in granules for oral use in constipation; or in powder form for douches (2 teaspoonfuls in 250 ml. of water) in the treatment of recto-colitis, sigmoiditis, etc.

### Spleen Substance Desiccated.

**Dose.**—5 to 10 grains (0.3 to 0.6 g.). 1 part represents 5 of the fresh spleen. Has been used in anæmia, tuberculosis, myxœdema, etc. Value in typhoid and malaria possibly due to splenic hormones.

Extract of pig's spleen stated to give 100% of recoveries in tuberculosis of first degree and 75% in all—several hundred cases treated since 1903. One or two injections of 5 ml. intramuscularly (thigh) or subcutaneously (abdomen) daily for adults. Oral route (in syrup) for prophylaxis, or adjuvant to injections; 4 tablespoonfuls given daily with meals to adults, representing 25 g. spleen tissue. Dose injected, or *per os*, proportionally less for children. Treatment absolutely harmless.—Baile, *per J. Amer. med. Ass.*, ii/1925, 1434.

Calcium metabolism stimulated by spleen, preparing suitable calcium salts for the blood stream and body cells. Splenic and parathyroid extracts suggested for treatment of pulmonary tuberculosis.—*per Prescriber*, 1926, 227.

Spleen extract is a valuable adjuvant in the treatment of chronic malaria. It increases organic immunity, stimulates the reticulo-endothelial system and phagocytosis, improves the blood condition and general nutrition, and effects a marked reduction in the size of the spleen. It has no direct action on the malaria parasite and none on the fever.—A. Mangiacapra, *per Trop. Dis. Bull.*, 1937, 619.

**Splenex (Plasmon, London).** A liquid extract of spleen substance (4 oz. = 2½ lbs. raw spleen), sweetened and flavoured. **Dose.**—½ to 1 tablespoonful daily for 3 weeks, with a week's interval between courses.

**Splenoxoid (Oxo, London).** Liquid extract of spleen. Treatment of tuberculosis of lungs, bones, and joints, and of polycythemia.

### Extracts of Muscle and Other Tissues.

Several preparations stated to cause vasodilatation have been suggested for use in the treatment of hypertension, angina pectoris and intermittent claudication. The substances employed for this purpose include extracts from striated muscle, liver, kidney, pancreas and urine. The nature of the active principles in these substances is still a matter of controversy.

According to Frey (1926) there is excreted in the urine a substance which has a pronounced effect on the cardiac rate and amplitude, and on the flow of blood through the coronary vessels. This substance is believed by Frey to be derived from certain tissues, especially the pancreas, and to be a specific "cardiac hormone." It is present in the blood, but in an inactive form which can easily be converted into the active form. It is present in smaller amounts in extracts of other tissues. When the pancreas is removed the amount of cardiac hormone excreted in the urine is reduced to about 20% of the amount normally excreted. Haberlandt in 1924 showed the presence in heart muscle of a substance which had a stimulating effect on the heart beat, and Schwartzman showed that extracts of skeletal muscle have a similar effect.

Extract of heart muscle in angina pectoris and intermittent claudication.—M. S. Schwartzman, *Brit. med. J.*, i/1930, 855; *ibid.*, i/1931, 493.

Intermittent claudication well treated by Lacarnol and Padutin.—M. Newman, *Brit. med. J.*, i/1933, 611. See also *Brit. med. J. Edit.*, i/1931, 82.

All have essentially similar action; none can replace digitalis in myocardial weakness or cardiac irregularity. Use not entirely without risk and caution necessary. Precise use and limitations still to be determined.—*Lancet*, ii/1931, 28.

Frey's hormone injected into the jugular vein produces a quick and sharp fall in systemic blood volume. At the same time it increases the relative coronary outflow. The effects of muscle extract are very similar to those of pancreatic tissue extract, but more pronounced.—C. W. Greene, *J. Pharmacol.*, 1936, 57, 98.

[P1-81-84] **Angiolysin** (Coates & Cooper, London). Tablets contain adenosine-phosphoric acid 0.0012 g. and pyrrhodid (amidopyrine-rhodan compound) 0.125 g. In angina pectoris.

**Angioxyl** (Roussel Laboratories, London). An insulin-free extract of pancreas for treatment of hypertension. In 2 ml. ampoules for intramuscular injection, 1 to 4 times daily; also as a syrup for oral administration.

**Cardone** (Paines & Byrne, London). Muscle extract from heart and skeletal muscle, and also from the liver and pancreas. *Dose*.—10 to 25 drops on a lump of sugar 1 to 3 times daily before meals, or 1 ml. once or twice daily intramuscularly. Angina pectoris, vascular disease, etc.

**Lacarnol** (Bayer Products, London). A nucleoside preparation from organic tissues. *Dose*.—10 to 25 drops per os 1 or 3 times daily; 1 ml. once or twice daily subcutaneously or intramuscularly. In angina pectoris and allied vascular diseases when due to arteriospasm.

**Manetil** (Bayer Products, London). An extract of spinal cord having the property of decreasing the bleeding-time without exerting a specific effect on the rate of coagulation. It is supplied in dry ampoules with ampoules of sterile water, the solution being administered intramuscularly, and is standardised by tests on mice. Of value in all forms of hæmorrhage. *Dose*.—1 to 3 ampoules during 24 hours is usually sufficient; more may safely be given.

**Padutin** (Bayer Products, London). Preparation of a vasomotor hormone obtained from pancreas. For oral or intramuscular use in angiospasm, Raynaud's disease, and generally for regulating blood pressure.

**Vagotonine** (Byla, Paris; Anglo-French Drug Co., London). Preparation of a pancreatic hormone available in ampoules (0.02 g.) and tablets (0.025 g.). For arterial hypertension and paroxysmal tachycardia.

## HEXAMINA

B.P.



*Syn. and Prop. Names.* HEXAMETHYLENETETRAMIN (P.G. VI, Fr. Cx.), HEXAMETHYLENAMINA (P. Helv. V, P. Dan., P. Ned. V, P. Jap., F.E. VIII, P. Belg. IV, P. Ital. V), METHENAMINA (U.S.P. XI), UROTROPINE, AMINOFORM, FORMIN, FORMAMINE, URISOL, METRAMINE (Oppenheimer, London), URITONE, VESALVINE (Martindale, London).

The trade-mark "Urotropine," No. 215652, was "avoided" in Gt. Britain by order of the Board of Trade.

*Dose*.—10 to 30 grains (0.6 to 2 g.) in a large volume of water. Very large doses may be given in conjunction with alkalis when not administered for urinary infections (*vide infra*). U.S.P. XI average dose 5 grains.

P. Ned. V max. single dose 1 g.; max. daily dose 4 g. For children, 3 to 4 grains in water to 5 times during the day.

*Intravenously*.—75 minims (5 ml.) of 40% solution. Larger doses have been given.

Colourless crystals, sublimable.

*Soluble* 1 in  $1\frac{1}{2}$  of water giving alkaline solution. 1 in 8 of alcohol 90%, 1 in 12 of chloroform; almost insoluble in ether.

It burns with intense heat and without soot. A 5-grain tablet will boil a test tube half-full of water.

**DECOMPOSITION ON STERILISATION.** 25 and 40% solutions in ampoules were sterilised by tyndallisation at 60°, heating in steam for 30 minutes, and autoclaving at 110° for 15 minutes; other ampoules were unsterilised. After 3 months the free formaldehyde was determined colorimetrically by means of 1% phloroglucin in 33% potassium hydroxide solution; the pH of the solutions was also determined. Unsterilised 25% solutions showed 0.0688% of formaldehyde, with pH 9.50; tyndallised solutions contained 0.0882%, pH 9.81; steam sterilised solutions contained 0.125%, pH 10.12; autoclaved solutions contained 0.115%, pH 10.01. Results with 40% solutions were similar. Additions of gelatin, 1 or 2%, reduced the decomposition due to heat.—G. Toni, per *Quart. J. Pharm.*, 1937, 119.

**Antiseptic Powers.** Hexamine itself is not antiseptic if the liberation of formaldehyde is prevented by the presence of alkalis, and the antiseptic action is always parallel to the concentration of free formaldehyde. Although the amount of formaldehyde liberated from therapeutic doses of hexamine cannot be sufficient to kill *B. coli*, slow generation by the drug in the presence of an acid inhibits bacterial growth. It is necessary therefore to raise the acid index of the urine within reasonable limits.

Hair, Lepper and Martland found the greatest concentration of H-CHO in the urine, after giving hexamine, was 1 in 20,000, whereas anything less than 1 in 5000 is said not to be bactericidal. They found that only when the pH of the urine had fallen to 4 are effective doses of H-CHO liberated. The urine should be collected under toluene and the pH tested with phenol red.—D. Nabarro, *Brit. med. J.*, ii/1930, 417.

**Toxic Effects.** Though hexamine itself is non-irritant, large doses, with consequent liberation of comparatively large amounts of formaldehyde, may give rise in susceptible individuals to painful micturition, cystitis and hæmaturia.

Doses of 15 to 30 gr., although official, if given alone or with sodium acid phosphate, are liable to cause hæmorrhagic cystitis.—A. F. Hurst, *Pharm. J.*, ii/1934, 676.

Hæmaturia caused in a case of acute encephalitis due to hexamine in doses of 20 gr. every 6 hours.—Sir Thomas Horder, *Brit. med. J.*, i/1927, 995.

**Uses.** Hexamine is one of the most effective of the urinary antiseptics, though it has been to some extent superseded during recent years by mandelic acid and sulphanilamide (*q.v.*). Since its antiseptic action is only exerted in an acid urine it is usually administered in conjunction with sodium acid phosphate, which is preferably given in a dose of 1 or 2 g. an hour or so before the hexamine.

Hexamine is of value in the treatment of cystitis, pyelitis, urinary retention, and in the pyuria of tabes dorsalis. It is a valuable drug in chronic cholecystitis and, combined with biliary drainage, it forms the most effective method of treatment in the majority of cases; for this purpose large doses of hexamine are given with simultaneous administration of *alkalis* (*vide infra*).

In a dose of 10 gr. three times daily hexamine has been employed in the treatment of typhoid carriers, on the theory that the bacilli are harboured in the gall-bladder and passed out in the urine.

**CHOLECYSTITIS.** It has been shown by Knott that bile obtained through a duodenal tube, after the administration of large doses of hexamine, is strongly antiseptic, although alkaline. Formerly the maximum dose of hexamine which could be given with safety was limited by the supposed necessity for keeping the urine acid, but just as efficient an action as a biliary antiseptic can be obtained



when sufficient alkali is given to prevent the formation of formaldehyde. Under such conditions enormous doses of hexamine can be given without causing any bladder irritation. A mixture containing 60 gr. each of sodium bicarbonate and sodium citrate is given after breakfast, after tea and the last thing at night after drinking a glass of milk or water. The reaction of the urine is tested every time it is passed; as soon as it is found to be constantly alkaline, if necessary after the dose of alkalis has been increased, 100 gr. of hexamine is added to the mixture, so that 300 gr. is given daily. The treatment can be continued for six weeks. The hexamine sterilises the bile ducts and gall-bladder, and when combined with non-surgical biliary drainage by means of Epsom salts, it results in the cure of most cases of cholecystitis. This treatment should be given for a week or two before and after operations on the gall-bladder and bile ducts in order to guard against septic complications. In severe infective cholangitis with jaundice, high temperature and rigors, it has appeared to save life.

**CHOREA** in children well treated intravenously. In one case 18 injections, increasing from 2 to 6 ml. of a 5% solution, were made in 6 weeks. More recently 10% solution has been used with good results.—*Per J. Amer. med. Ass.*, ii/1925, 1098. Seems to give best results by intravenous injection when the chorea is associated with an infection, e.g., encephalitis or polyarthritis.—*De Capua, J. Amer. med. Ass.*, ii/1929, 808.

**PYELITIS.** In the acute stages of severe pyelitis 5 ml. of 40% solution intravenously once or twice daily till temperature falls exceedingly effective.—*Hamilton Bailey, Practitioner*, i/1933, 346.

Hexamine in well acidified urine cures at least one third of the cases of non-surgical pyelitis and cystitis, but there is no method of determining which case will respond.—*D. R. Mitchell and J. M. Scott, Brit. J. Surg.*, 1933, 225.

**PYELITIS OF PREGNANCY.** A single injection of 10 ml. of the solution is often sufficient.—*A. Jacobs, Practitioner*, ii/1927, 219.

**RETENTION OF URINE** has been treated by 5 to 10 ml. of 40% hexamine solution intravenously.

**TYPHOID.** 20 grains or more 3 times in 24 hours with an equal quantity of sodium citrate and sodium bicarbonate, starting from the beginning of the second week onwards. If cholecystitis appears give 10 20-gr. doses with sufficient alkali in 24 hours and apply Antiphlogistine over gall-bladder region.—*A. E. Gow, Lancet*, i/1930, 96.

**Mistura Hexaminæ (U.C.H.).** No. 1: Hexamine 10 gr., chloroform water to 1 dr. half an hour before food; No. 2: Sodium acid phosphate 30 gr., chloroform water to 1 dr. half an hour after food.

**Tabellæ Hexaminæ (B.P.C.)** contain 5 gr. (0.3 g.).

**Tabella Hexaminæ Composita (C.X.H.).** Hexamine 4 gr., sodium glycocholate 1 gr., sodium taurocholate 1 gr., sodium salicylate 5 gr. *Dose.*—1 or 2 tablets.

**Acitetramin (Richter, London).** Hexamine acid phosphate. *Dose.*—1 or 2 8-grain tablets 3 times a day. Urinary antiseptic; contraindicated in tuberculous cystitis.

**Coerulamin (Richter, London).** Hexamine acid phosphate 0.1 g., methylene blue 0.02 g. per tablet. *Dose.*—2 to 3 tablets daily. Also issued in ampoules containing hexamine 32 gr., methylene blue  $\frac{1}{2}$  gr. *Dose.*—3 to 6 per week by intravenous injection. For pyelitis, nephritis, gonorrhœa, etc.

**Cylotropin (Schering, London).** Ampoules of 5 ml. contain 30 gr. of hexamine, 12 gr. of sodium salicylate, and 3 gr. of caffeine sodium salicylate. *Dose.*—5 ml. intravenously or intramuscularly daily or on alternate days. In infective urinary conditions.

**Mirion (Schering, London).** A preparation of hexamine with organic iodine for injection in ampoules containing 1 and 3 ml. For use in arthritis deformans, surgical tuberculosis, prostatitis, epididymitis, etc.

**Solvurate (Richter, London).** Granules containing in 5 g.: hexamine 0.4 g., piperazine 0.1 g., lithium carbonate 0.05 g., sodium benzoate 0.05 g. *Dose.*— $\frac{1}{2}$  oz. thrice daily. Pyelitis, renal calculus.

**Uraseptine (Rogier, Paris; Anglo-French Drug Co., London).** Granules of hexamine and hexamine citrate, with benzoates and diethylenediamine. *Dose.*—3 to 6 teaspoonfuls daily. Urinary antiseptic and in the uric acid diathesis.

**Hexamine Benzoate.**  $(\text{CH}_2)_6\text{N}_4 \cdot \text{C}_6\text{H}_5 \cdot \text{COOH} = 262.2$ .

*Dose.*—5 to 15 grains (0.3 to 1 g.).

Small scaly crystals containing about 53% of the base. Made by combining equivalent quantities and crystallising. Soluble 1 in 50 of water and 1 in  $2\frac{1}{2}$  of alcohol 90%.

*Uses.* A urinary antiseptic.

**Cystazol** (*Allen & Hanburys, London*). Hexamine sodio-benzoate in 10 gr. tablets. *Dose.*—1 to 3 dissolved in water twice or thrice daily, in bacterial infections of the urinary tract. Also available in effervescent granules.

**Uro-Hexoids** (*British Drug Houses, London*). Tablets of hexamine and lithium benzoate. *Dose.*—1 or 2 after each meal, taken whole or crushed and dissolved in water. Urinary antiseptic, diuretic and anti-lithic.

**Hexamine Camphorate.** *Prop. Name.* AMPHOTROPIN (*Bayer Products, London*).  $[(\text{CH}_2)_6\text{N}_4]_2 \cdot \text{C}_6\text{H}_{14}(\text{COOH})_2 = 480.4$ .

*Dose.*—8 to 12 grains (0.5 to 0.8 g.). Tablets 8 grains (0.5 g.).

A white crystalline powder made by combining in alcohol, chloroform, etc.

*Soluble* in water 1 in 10 with acid reaction. Solutions are hydrolysed to a great extent.

*Uses.* Urinary antiseptic. An alkaline urine is rendered neutral or acid by administration. In chronic cystitis, bacilluria, nephritis.

**Amphotropin Solution** (*Bayer Products, London*). 40% solution of hexamine camphorate. For intravenous injection in urinary affections.

**Hexamine Salicylate.** *Syn. and Prop. Name.* VESALVINE "S" (*Martindale, London*), SALURENE.  
 $(\text{CH}_2)_6\text{N}_4 \cdot \text{C}_6\text{H}_4 \cdot \text{OH} \cdot \text{COOH} = 278.2$ .

*Dose.*—5 to 15 grains (0.3 to 1 g.) in water before meals.

Colourless prismatic crystals with agreeable sweetish saline taste, containing approximately 50% of each constituent. Prepared by combining equimolecular proportions.

*Soluble* 2 in 1 of water and 1 in 2 of alcohol. A saturated aqueous solution will remain clear for months, whilst vigorous rubbing on the sides of the vessel will cause a deposition of salicylic acid crystals.

*Incompatible* with acids, alkalis, carbonates and salicylates, hence best administered alone. It decomposes on heating in water or alcohol.

*Uses.* A urinary and intestinal antiseptic in cystitis, bacilluria, gastro-intestinal catarrh, colitis, dysentery, diarrhoea, dyspepsia, and all cases beneficially treated by hexamine. It splits up on passing through the system into its two constituents—the salicylic acid enhancing the effect of the hexamine. It does not irritate the bladder like other antiseptics.

**Neohexal** (*Riedel-de Haen, Berlin; Endocrines-Spicer, Watford*). Combination of hexamine and sulphosalicylic acid in 0.5 g. tablets. *Dose.*—1 or 2 tablets dissolved in water thrice daily. Affections of the urinary tract.

**Hexamine Sodium Acetate.**

$(\text{CH}_2)_6\text{N}_4 \cdot 2\text{CH}_3\text{COONa} \cdot 6\text{H}_2\text{O} = 412.3$ .

*Dose.*—30 grains (2 g.). A crystalline salt made by evaporating

solutions of the components in the above proportions. Contains approx. 34% of hexamine. In gonorrhœa and cystitis.

**Cystopurin Tablets** (*Genatosan, Loughborough*). Contain 1 g. of hexamine sodium acetate.

**Hexamine Triborate.** *Prop. Name.* BOROVERTIN (*Bayer Products, London*) (*P. Ned. V.*).  $(\text{CH}_2)_6\text{N}_4 \cdot 3\text{HBO}_2 = 271.9$ .

*Dose.*—15 to 60 grains (1 to 4 g.) daily.

Crystalline powder containing about 50% of hexamine, made by combination of 1 mol. of hexamine and 3 mols. of boric acid. Soluble in water 1 in 13. Urinary antiseptic, *e.g.*, in gonorrhœal cystitis, pyelitis, renal calculus and tuberculosis of the bladder and kidneys.

**Formamol (B.P.C.).** *Syn. and Prop. Name.* HEXAMINE ANHYDROMETHYLENECITRATE, HELMITOL (*Bayer Products, London*).

*Dose.*—8 to 15 grains (0.5 to 1 g.). White crystals soluble 1 in 5 of water, sparingly soluble in alcohol. Is similar to hexamine in its action and is used in infections of the genito-urinary tract.

**Neotropin** (*Schering, London*). Butyloxydiamino-azopyridine. A urinary antiseptic for oral use. *Dose.*—Two dragees (each 0.1 g.) three times a day. Urinary tract infections, cystitis, pyelitis, etc.

**Pyridium** (*Pyridium Corporation, New York; Menley & James, London*) is phenyl-azo-alpha-diamino-pyridine hydrochloride. A red, microcrystalline powder, slightly soluble in water, readily soluble in hot water. *Dose.*—3 gr. 3 times daily. In hyperacidity dose should be regulated and given immediately after meals. It possesses anti-bacterial action against cocci and *B. coli*, and is eliminated through the genito-urinary tract. Is used in gonorrhœal infections, *B. coli* and mixed infections, pyelitis and cystitis. Also used locally as antiseptic in the form of a 1% solution, or ointment (10%).

**Contraindications.** Idiosyncrasy towards the compound when given internally is indicated by colic, nausea, headache and vertigo; reduced dosage may, however, establish tolerance, but if not discontinue. Kidney disease is a contraindication, and it should not be given in severe hepatitis, where excretion is slow, nor in uræmia. Use with caution in severe chronic gastro-intestinal disorders. The compound should not be used simultaneously with mercurial irrigations.

## HYDRARGYRUM

B.P., U.S.P. XI, Fr. Cx., P. Jap. V, P. Helv. V, P. Dan.

Hg = 200.61.

[P1] "Mercury, oxides of; nitrates of mercury; mercuric ammonium chlorides; potassio-mercuric iodides; mercuric oxycyanides; mercuric thiocyanate."

[P2] "Mercuric chloride; mercuric iodide; organic compounds of mercury."

[S1] "Mercuric chloride except substances containing less than 1% of mercuric chloride; mercuric iodide except substances containing less than 2% of mercuric iodide; nitrates of mercury except substances containing less than the equivalent of 3%, weight in weight, of mercury (Hg); potassio-mercuric iodides except substances containing less than the equivalent of 1% of mercuric iodide; organic

*compounds of mercury except substances containing less than the equivalent of 0.2%, weight in weight, of mercury (Hg)."*

[83] "*Mercuric chloride—in batteries.*"

"*Mercuric chloride; mercuric iodide; organic compounds of mercury—in dressings on seeds or bulbs.*"

"*Mercury, nitrates of—in ointments containing less than the equivalent of 3%, weight in weight, of mercury (Hg).*"

[86] "*Mercury, organic compounds of—specify proportion as the proportion of organically-combined mercury (Hg) contained in the preparation.*"

*Dose.*— $\frac{1}{2}$  to 3 grains (0.03 to 0.2 g.); by intramuscular injection,  $\frac{1}{2}$  to 1 grain (0.03 to 0.06 g.).

Mercury has a sp. gr. of about 13.5, a f.p. of  $-38.8^{\circ}$  and a b.p. of about  $358^{\circ}$ .

**Antidotes to Acute Poisoning by Mercurial Salts.** Give raw white of egg in water in unlimited quantities, but remove it from the stomach as soon as possible by emetic or stomach tube, as albuminate of mercury formed is soluble in excess of albumin and sodium chloride. It is now stated by many authorities that medicinal charcoal in suspension is much more efficacious than white of egg; it should be given and quickly removed, as above.

Discussed point as to whether to give antidote or emetic first—probably best to give whichever comes first to hand, but it is important to remember that much white of egg may lessen efficacy of emetic.

Keep patient warm; give brandy,  $\frac{1}{2}$  oz., or aromatic spirit of ammonia,  $\frac{1}{2}$  dr., in water; alkalising demulcent drinks freely. Saline and 5% dextrose intravenously. Sodium thiosulphate intravenously said to be of doubtful value; sodium formaldehyde sulfoxylate more effective.

Sodium formaldehyde sulfoxylate said to be most efficient chemical antidote for mercuric chloride. Details of 10 cases treated. Suggested technique: gastric lavage with 5% solution, 200 ml. to be left in the stomach; 10 g. in 100 to 200 ml. of water intravenously slowly over 20 to 30 minutes. Later, after 4 or 6 hours, 5 to 10 g. intravenously repeated.—Rosenthal, *J. Amer. med. Ass.*, i/1984, 1277.

Sodium formaldehyde sulfoxylate is a powerful reducing agent more stable in the body than sodium thiosulphate and sodium hydrosulphite. Owing to its low toxicity as much as 10 to 15 g. may be given intravenously in 10% solution, 5 to 10% as gastric lavage, leaving 100 to 200 ml. in the stomach, and a 5% solution by enema. Treatment is repeated in severe, acute cases within 4 to 6 hours, and again in 24 hours. In 1 case reported, treatment consisted of 6 intravenous injections over a period of 4 days. In cases of severe poisoning with mercuric chloride, intravenous injection should be accompanied by oral use and enemas to avoid tissue destruction.—W. E. Robertson and V. L. Tuck, *per J. Amer. pharm. Ass.*, 1935, A-343.

Suggested that 10 ml. of 10% solution of sodium hypophosphite with 5 ml. of hydrogen peroxide in a glass of water, administered by mouth, and used for gastric lavage, is a suitable antidote for mercury poisoning.—J. R. Ross and A. Brown, *Canad. publ. Hlth J.*, 1935, 26, 237.

Immediate gastric lavage important, but subsequently of little effect—first lavage should be thorough. Enemas if diarrhoea is absent. Continuous intravenous drip saline useful, but waterlogging must be avoided.—*Lancet*, i/1936, 617.

Therapeutic effects of gastric lavage, alkalis and intravenous saline described—43 out of 46 cases of mercurial poisoning so treated recovered.—W. B. Porter and C. E. Simons, *Amer. J. med. Sci.*, 1934, 188, 375.

Massive alkalisation has given good results in treatment of acute mercurial poisoning during 8 years of trial.—Nanu-Muschel, V. Ciocalteu and C. Ciocalteu, *J. Prat., Paris*, Apr. 16., 1935.

Treatment of poisoning by mercuric chloride. Gastric lavage with saturated solution and colonic irrigation with 5% solution of sodium bicarbonate, internal administration of it in dosage sufficient to keep urine alkaline to litmus; 500 ml. of 5% solution intravenously after lavage.—*Brit. med. J.*, i/1935, 400G.

**Uses.** Mercury is used as a purgative, cholagogue and anti-syphilitic.

**Emplastrum Hydrargyri (B.P.C.)** contains about 33% of mercury. A more satisfactory preparation is produced by omitting the sulphur.

**Emplastrum Hydrargyri et Phenolis** contains about 20% of mercury and 3 to 5% of phenol in rubber adhesive plaster. The machine-spread plaster is usually made with about 4 ounces of mass per square yard spread on bleached cotton cloth of plain weave.

**Hydrargyrum cum Creta (B.P.).** *Syn.* GREY POWDER.

*Dose.*—1 to 5 grains (0.06 to 0.3 g.).

Contains 33% of mercury. Liable to oxidise in the air or during storage, but this can be prevented by the presence of certain sugars and the addition of 1% of dextrose has been recommended. A mild purgative, especially for children.

**Hydrargyrum cum Creta (U.S.P. XI).**

*Average dose.*—Laxative, 4 grains (0.25 g.). Mercury, honey and a little water shaken together for 10 hours or longer if necessary, chalk made into a paste with water, and the two parts then mixed and dried, first between bibulous paper and then in a dish at ordinary temperature.

**Injectio Hydrargyri (B.P.).** *Syn.* MERCURIAL CREAM.

*Dose.*—5 to 10 minims (0.3 to 0.6 ml.) by intramuscular injection. Weekly injections are given into the upper and outer quadrant of the gluteal region.

Contains about 10% w/v of mercury with camphor and creosote in wool fat and olive oil. *B.P. Add. III* allows the use of arachis oil, in place of olive oil, in making injection of mercury.

For combined treatment of syphilis with neoarsphenamine and mercury, see p. 231.

**Toxic Effects.** Malaise, stomatitis, dermatitis, nephritis and, rarely, colitis may occur. Malaise is an indication for a reduction in dosage. Stomatitis is the most common symptom. It may be prevented by oral hygiene and by the use of potassium chlorate lozenges. If necessary, sodium thiosulphate may be injected. Must be given with care to those with kidney disease, owing to the irritant action of mercury.

**Cremor Mercurialis (N.H.).** Staff Surgeon Adams' Formula.

*Dose.*—5 minims (= 1 grain of mercury) given once a week. Mercury 20, wool fat 30, chlorbutol 2, all by weight, liquid paraffin to 100 by measure.

**Injectio Hydrargyri Fortis (B.P.C.).** *Syn.* OLEUM CINE-REUM, GREY OIL.

*Dose.*—1 to 2 minims (by intramuscular injection). Contains 40% w/v of mercury.

**Huile Mercurielle** (*Fr. Cx.*). *Syn.* HUILE GRISE, OLEUM CINEREUM. Mercury 40, wool fat 26, Vaseline oil (*Fr. Cx.*) 55, guaiacol 2, camphor 3, all by weight. Measures 100, i.e., 40% *w/v* of mercury. *P. Ned. V* and *P. Belg. IV* are similar but without guaiacol and camphor. *F.E. VIII* is made with chloroform and contains castor oil, with guaiacol and camphor as preservatives.

Suppositories containing the 40% grey oil in various strengths have been used in syphilis. Efficacious, simple and safe.

**Lanolinum Hydrargyri.**

Mercury 100, lanolin (hydrous) 200, mercurial ointment 5, mutton suet 50. For inunction in syphilis (effect is rapid); used daily 4 to 8 times after a hot bath.

**Linimentum Hydrargyri (B.P.C.).**

Contains about 30% *w/v* of mercury ointment (equivalent to 9% *w/v* of Hg) with ammonia and liniment of camphor.

Useful stimulant for enlarged joints and glands.

[P2-81] **Massa Hydrargyri (U.S.P. XI).** *Syn.* BLUE MASS, BLUE PILL.

*Average dose.*—3 grains (0.2 g.).

Mercury 33, mercury oleate 1, liquorice 10, althea 15, glycerin 9, honey 32. Same strength as mercury pill, *B.P.*

**Pilula Hydrargyri (B.P.).** *Syn.* BLUE PILL.

*Dose.*—4 to 8 grains (0.25 to 0.5 g.).

Contains 33% *w/w* of mercury.

In raised arterial tension, when indicative of danger, a pill twice or thrice weekly, followed by saline, is beneficial.

In syphilis, begin with 1½ grains after the first and last meals, increasing the daily dose by 1 grain each week till patient is taking 2 grains thrice daily. An average dose is 2 grains twice a day.

In cardiac dropsy it seems to act complementarily to digitalis, and to prove efficient where latter has failed to increase urinary secretion materially. It is to be avoided if renal disease is present. When diuresis is fully established discontinue mercury and give a mixture of caffeine and spirit of nitre with infusion of scopolarium.

[P1-81] **Pilulæ Hydrargyri cum Creta et Opii (B.P.C.).** *Syn.* HUTCHINSON'S PILLS.

*Dose.*—1 pill. Contain 1 gr. of grey powder and 1 gr. of Dover's powder (*exempt* [D]). For syphilis; the opium tends to counteract the irritant action of the mercury.

For a preparation of similar composition also *exempt* [D] see p. 1140.

**Pilulæ Hydrargyri cum Rheo (B.P.C.).**

*Dose.*—1 pill. Contain 2½ gr. each of mercury pill and compound rhubarb pill.

**Unguentum Hydrargyri (B.P.).**

Mercury, 30% *w/w*, in suet and benzoinated lard. *B.P. Add. III* allows the use of sufficient white beeswax, in place of an equal weight of benzoinated lard, to produce an ointment of the required consistence. Principally used for inunction in syphilis; also to relieve local inflammation and to destroy pediculi.

*P. Svec.* contains Hydrargyrum Extinctum 36 (i.e., mercury "killed" by rubbing with wool fat, and containing 83.5% of Hg), benzoinated lard 44, suet 20, i.e., about 30% mercury.

For the inunction treatment of cerebrospinal syphilis, 5 g. of ointment should be rubbed firmly, but not vigorously, for 20 to 30 minutes on successive nights into alternately the thighs, buttocks, calves, abdomen, back, and chest. Following inunction the area should be covered with a piece of lint and lightly bandaged, the bandage being removed on the following night and applied to the area freshly treated. A bath should be taken once or twice a week and the treatment continued for three or four weeks or longer, care being taken to watch for signs of intolerance.

**Pommade Mercurielle Faible** (*Fr. Cx.*) contains 12½% of mercury in benzoinated lard.

**Pommade Mercurielle à Parties Égales** (*Fr. Cx.*). *Syn.* ONGUENT NAPOLITAIN. Mercury 1, benzoinated lard (containing 0.15% of added cholesterol) 1. [P1-81] **Pommade Mercurielle Belladonnée** (*Fr. Cx.*) contains mercury ointment (*Fr. Cx.*) 80, extract of belladonna 10, glycerin 10, by weight.

**P2-81 Unguentum Hydrargyri Forte** (*U.S.P. XI*). *Syn.* STRONG MERCURIAL OINTMENT.

Mercury 50, oleate of mercury 2, wool fat 30, white wax 5, white petrolatum 13.

### **Unguentum Hydrargyri Compositum (B.P.).**

Mercury ointment 10, yellow beeswax 6, olive oil 6, camphor flowers 3. Contains 12% of mercury.

*B.P. Add. II* allows the use of either arachis, cottonseed or sesame oil in place of olive oil in the preparation of compound mercury ointment.

For enlarged glands, chronic synovitis and syphilitic nodes. Swelling of the ankles is well treated with it. Is usually supplied for Scott's Dressing.

**Unguentum Mercuriale (B.P.C.).** *Syn.* UNGUENTUM HYDRARGYRI MITE, BLUE OINTMENT, TROOPER'S OINTMENT. A dilution of ointment of mercury 33½% with lard. Contains 10% Hg.

For destroying lice.

To promote the removal of the effusion of pleurisies, the rubbing into the chest of half a drachm of mercurial ointment twice daily is often useful.

**Unguentum Hydrargyri Mite (U.S.P. XI).** *Syn.* MILD MERCURIAL OINTMENT.

Strong mercurial ointment 60, white wax 2, white petrolatum 38.

### **Mercury Amalgam.**

This is one of the most popular of dental fillings. Black (*Cosmos*) suggests: Silver 68.5, tin 25.5, zinc 1, gold 5.

In use, the alloy is worked up in a glass mortar with an equal quantity of mercury, and the excess of mercury is squeezed out immediately before filling in. It is the general rule to employ a double filling, *i.e.*, to insert an initial filling of zinc oxysulphate or oxyposphate, and afterwards an amalgam when a metal filling is employed, and where depth of the cavity will allow.

Amalgam fillings of teeth may cause mercury poisoning in susceptible people.

[P1] **Hydrargyrum Ammoniatum (B.P., U.S.P. XI, P. Svec. X, P. Ned. V, P. Jap. V).** *Syn.* MERCURIC AMMONIUM CHLORIDE, WHITE PRECIPITATE.  $\text{NH}_2\text{HgCl} = 252.1$ .

A white powder obtained by the interaction of ammonia and mercuric chloride, insoluble in water but soluble in hydrochloric

acid. On prolonged contact with water a yellow basic salt is produced.

[P1] **Unguentum Hydrargyri Ammoniat** (*B.P.*).

Strength 5% in simple ointment.

In pruritus and other skin affections.

[P1] **Unguentum Hydrargyri Ammoniat Dilutum** (*B.P.C.*). Equal parts of the *B.P.* ointment and simple ointment.

Pustular eczema, resulting from pediculosis capitis in weakly children, is well treated with equal parts of this ointment and olive oil, enclosing the head in an oiled paper cap.

[P1] **Unguentum Hydrargyri Ammoniat et Zinci Oxidi** (*B.P.C.*). Equal parts of ointment of ammoniated mercury and ointment of zinc oxide.

[P1] **Unguentum Hydrargyri Ammoniat** (*U.S.P. XI*).

Ammoniated mercury 10, wool fat 5, white wax 5, white petrolatum 80.

*Tinea circinata* can be rapidly cured by this ointment.

[P1] **Hydrargyri amido chloridum pultiforme** (*P. Dan.*) is a 20% paste of freshly precipitated ammoniated mercury in wool fat and white soft paraffin for preparing ointments.

[P1] **Unguentum Hydrargyri cum Paraffino** (*St. G.H.*). Ammoniated mercury 12 gr., oil of geranium 4 m., yellow soft paraffin to 1 oz. To be used sparingly with a camel hair brush, to the nose.

[P2-S1] **Hydrargyri Benzoas.** *Syn.* MERCURIC BENZOATE.

$(C_6H_5COO)_2Hg, H_2O = 460.7$ .

*Dose.*—*Per os*,  $\frac{1}{16}$  to  $\frac{1}{8}$  grain (0.0025 to 0.006 g.); by hypodermic injection—a daily dose of 1 to 2 ml., rising to 5 ml., of a 1% solution, made with the aid of 0.75% of sodium chloride in water; in preference with the addition of 0.75 to 1% of cocaine hydrochloride. Or weekly, 0.25 g. in 10% paraffin suspension.

A white crystalline powder, practically insoluble in cold water, but soluble with addition of salt, also soluble about 1 in 180 of alcohol 90%. Has been used for treatment of syphilis and as a urethral injection (1 in 2000 to 1 in 1000 in gonorrhœa).

**Hydrargyri Bromidum.** *Syn.* MERCURIC BROMIDE.  $HgBr_2 = 360.4$ .

*Dose.*— $\frac{1}{16}$  to  $\frac{1}{8}$  grain (0.004 to 0.016 g.). Silvery scales. Soluble 1 in 250 of water, decomposes on boiling.

In syphilis, in solution with sodium bromide thus:—Mercuric bromide 1.8 g., sodium bromide 1.03 g., water 100 ml., is employed in dose of 1 to 2 ml. of the solution (= 0.01 to 0.02 g. Hg) intramuscularly into the buttock. A platinum-iridium needle is essential. Some pain may be caused.

[P1-S1] **Hydrargyri Cyanidum** (*B.P.C., Fr. Cx., P.G. VI, P. Belg. IV*). *Syn.* MERCURY CYANIDE, CYANURETUM HYDRARGYRI.  $Hg(CN)_2 = 252.6$ .

*Dose.*— $\frac{1}{16}$  to  $\frac{1}{8}$  grain (0.004 to 0.008 g.). *Fr. Cx.* has max. single dose  $\frac{1}{8}$  grain, max. during 24 hours  $\frac{1}{4}$  grain approximately.

*Intravenous dose.*—1 ml. of 1% solution considered a max. single dose, but more has been given, *see below*.

White or colourless, prismatic crystals. *Soluble* 1 in 13 of water, 1 in 3 of hot water, 1 in 4 of glycerin and 1 in 20 of alcohol 90%. It is not decomposed by alkalis.

*Uses.* It is used as a lotion to syphilitic sores, and given in pills of  $\frac{1}{16}$  gr. twice daily. Has also been employed intravenously in syphilis, in 1% solution, in association with neoarsphenamine, and intravenously or intramuscularly, in doses of 0.04 to 0.05 g., as a diuretic in cardiac disease. Used in diphtheria,  $\frac{1}{8}$  to  $\frac{1}{4}$  gr. frequently, with 1 m. of tincture of aconite in honey, employing also a gargle, 1 in 10,000. Solutions of 1 in 1000 have been used in ophthalmia.



ACUTE SYPHILITIC NEPHRITIS. Albuminuria disappeared after 15 days treatment with intravenous injections of 0.005 to 0.02 g., thus rendering possible the use of arsenic and bismuth, which were previously contraindicated.—Petges, *J. Amer. med. Ass.*, i/1929, 1488.

[P1-S1] **Hydrargyri et Zinci Cyanidi (B.P.C.).** *Syn.* MERCURO-ZINC CYANIDE, LISTER'S SALT.

A white powder, sometimes supplied tinted with rosalane (mauveine hydrochloride), obtained by precipitation from a cold saturated solution of the cyanide of mercury and potassium by adding a cold saturated solution of zinc sulphate in equimolecular proportions, or by adding in similar solutions mercuric chloride to zinc potassium cyanide. The maximum percentage of mercuric cyanide found is 38.5, and the body is usually regarded as an intimate mixture of the constituent cyanides.

**Solubility.** Very slight in water, more so in dilute acids.

[P1] **Carbasus Hydrargyri et Zinci Cyanidi (B.P.C.).** *Syn.* DOUBLE CYANIDE GAUZE. Contains 0.5 to 1.5% of Hg, as  $\text{Hg}(\text{CN})_2$ , and 1.5 to 3.0% of Zn, as  $\text{Zn}(\text{CN})_2$ . It is a popular dressing for applying direct to wounds. It is not so irritant as some of the other mercurial dressings, and has the advantage of keeping well without the mercurial salt becoming reduced by the cotton. It may be damped before use with 1 in 20 phenol solution. Double cyanide wool and bandages contain the equivalent of about 3% of the double salt.

[P1] **Curatio Normalis I (B.P.C. Supp.).** *Syn.* STANDARD DRESSING NO. 1, DOUBLE CYANIDE DRESSING.

Mercury and zinc cyanide gauze 36 inches by 12 inches, absorbent cotton wool 180 gr., and an open-weave bandage 1 inch by 3 yards. It must be supplied in a sterile condition in the original sealed packets.

When this dressing is supplied for *N.H.I.* purposes the following directions must be clearly shown on the label:—"Directions for use. In the absence of any special directions by the doctor, the dressing should be used as follows:— (1) Cleanse the wound with plain boiled water or antiseptic solution; (2) apply the gauze so as to cover the wound; (3) apply the cotton wool so as to cover and overlap the gauze; and (4) apply the bandage."

[P1-S1] **Mercury and Zinc Cyanide Cream** may be made by triturating the powder with carbolic lotion 1 in 20 *g.s.*, for applying to hairy parts adjacent to wounds.

[P1-S1] **Mercury and Zinc Cyanide Paste.** Mercury and zinc cyanide 400, tragacanth 2, phenol 20, water 800, mix. For a first dressing for wounds. *Caution:* Not to be supplied in metal tubes—especially lead. The paste must be rubbed on in as thin a layer as possible.

[P1-S1] **Mercury and Zinc Cyanide Lotion**, of strength 1 in 5000 to 1 in 1000, is used for wounds. *Caution:* Shake bottle—not dissolved.

**Hydrargyri Iodidum Flavum (B.P.C., U.S.P. XI, Fr. Cx., P. Jap. V, P. Helv. V).** *Syn.* YELLOW MERCUROUS IODIDE.  
 $\text{HgI} = 327.5$ .

**Dose.**— $\frac{1}{2}$  to  $\frac{1}{2}$  grain (0.008 to 0.03 g.). *U.S.P. XI* average dose

$\frac{1}{2}$  grain. *Fr. Cx.* and *P. Helv.* *V* have max. single dose approx.  $\frac{1}{2}$  grain, max. per day 3 grains.

Prepared by double decomposition between solutions of mercurous nitrate and potassium iodide. (Must not be confounded with the yellow variety of mercuric iodide).

Pills and tablets contain  $\frac{1}{2}$  grain. Employed in syphilis.

[P1-81] *Pilules d'Iodure Mercureux Opiacées* (*Fr. Cx.*). *Syn.* RICORD'S PILLS.

Fresh mercurous iodide 0.05 g., opium 0.02 g., liquorice root 0.03 g. Mass with honey to make one pill (*exempt* [D]).

[P2-81] *Hydrargyri Iodidum Rubrum* (*B.P., Fr. Cx., P. Helv. V, P. Dan.*). *Syn.* MERCURY BINIODIDE, MERCURIC IODIDE, HYDRARGYRUM BINODATUM (*P. Jap. V*).  $HgI_2 = 454.5$ .

*Dose.*— $\frac{1}{2}$  to  $\frac{1}{16}$  grain (0.002 to 0.004 g.). *Fr. Cx.* has max. single dose  $\frac{1}{2}$  grain; max. during 24 hours  $1\frac{1}{2}$  grains approximately.

*Intravenously.*— $\frac{1}{2}$  grain (0.005 g.) in 75 minims (5 ml.) is usual, but  $\frac{1}{2}$  grain (0.03 g.) in 150 minims (10 ml.) has been given.

—See R. L. Spittel's formula below.

Red powder, *soluble* in solutions of other iodides, and in solution of mercuric chloride, forming double salts, *cf.* mercuric potassium iodide; also 1 in 230 of olive oil, 1 in 25 of castor oil (100 parts of the latter will dissolve 8 of this iodide with 5 of mercuric chloride), about 1 in 150 of ether, 1 in 300 of alcohol 90%.

*Uses.* A powerful antiseptic, less irritant than mercuric chloride. As a lotion for the hands or eyes 1 in 5000. For wounds 1 in 7000, vaginal douche 1 in 10,000.

More potassium iodide must be used to dissolve mercuric iodide than is indicated by the formation of the compound  $HgI_2 \cdot 2KI$ , otherwise  $HgI_2$  is precipitated on standing; at least an equal weight of potassium iodide should be used.

The strength of biniodide preparations should be expressed in terms of the active constituent,  $HgI_2$ . Statements of strength based on the theoretical content of double salts such as  $HgI_2 \cdot 2KI$ , or  $HgI_2 \cdot KI \cdot 1\frac{1}{2}H_2O$  are misleading. A 1 in 1000 solution of  $HgI_2 \cdot 2KI$  is equivalent to less than 1 in 1700 of biniodide, and 1 in 1000 of  $HgI_2 \cdot KI \cdot 1\frac{1}{2}H_2O$  is equivalent to less than 1 in 1400.

If a douche is required in midwifery, 1 in 1000 biniodide always used.—A. P. Murtz, *Lancet*, ii/1926, 728.

[P1] *Injectio Hydrargyri Iodidi Rubri* (Ragazzoni).

*Dose.*—2 to 6 minims (0.12 to 0.4 ml.).

Mercuric iodide 1 gr., sodium iodide *q.s.*, in 64 m.

In syphilis can be used in large doses, but is painful.

[P2] *Injectio Hydrargyri Iodidi Intravenosa* (R. L. Spittel).

*Dose.*—120 to 180 minims (8 to 12 ml.).

Mercuric iodide 3.24 g., sodium or potassium iodide 28.42 g., N/1 sodium hydroxide 40 drops or *q.s.*, water to 1000 ml. The solution is carefully rendered neutral, using phenolphthalein, the soda being added last. Often a single injection will produce an effect as marked as arsphenamine. Used in conjunction with latter in syphilis. *Caution:* An average dose of this contains 0.03 g. ( $\frac{1}{2}$  grain).

[P2] *Soluté Injectable d'Iodure Mercurique* (*Fr. Cx.*).

Mercuric iodide 1%, sodium iodide 1%, sodium chloride 0.7% in distilled water. Sterilise in the autoclave for 20 minutes at 110°.

**[P1-S1] Injectio Hydrargyri Biniodidi (pro vagina).**

Mercuric chloride 8 gr., potassium iodide 24 gr., water to 1 oz. 1 drachm of this to a pint makes 1 in 10,000 approx.

**[P1] Lotio Hydrargyri Biniodidi (L.H.).**

Mercuric chloride 3 gr., potassium iodide 8½ gr., alcoholic solution of rosolic acid *q.s.*, distilled water to 10 oz. Strength of double salt 1 in 500.

**[P1] Lotio Hydrargyri Biniodidi Spirituosus. Syn. BINIODIDE SPIRIT LOTION.**

Mercuric iodide 1, potassium iodide 1, alcohol 70% to 1000. For gonorrhœa dilute solutions are used, also as a pigment or spray for throat in scarlatina and diphtheria.

**[P1] Mistura Hydrargyri Biniodidi (K.C.H.).**

Dose.—1 ounce (30 ml.).

Solution of mercuric chloride 30 m., potassium iodide 10 gr., ammonium carbonate 5 gr., decoction of cinchona to 1 oz.

[P1] U.C.H. has solution of mercuric chloride 60 m., potassium iodide 4 gr., water to 1 oz.

**[P1] Mist. Hydrarg. et Pot. Iod. (N.I.F.).**

Solution of mercuric chloride 1 dr., potassium iodide 5 gr., concentrated infusion of calumba 30 m., water to ½ oz.

The mercury in these mixtures is more rapidly eliminated than when given alone. The potassium iodide acts as a diuretic.

**[P1-S1] Pilula Arsenii et Hydrargyri Iodidi.**

Dose.—1 or 2, two or three times a day.

Arsenious iodide, mercuric iodide, of each 1 gr., distilled water *q.s.* to dissolve, sugar *q.s.* to make 12 two-grain pills. May be combined with 2 gr. of iodide of iron.

**[P2-S1] Pilula Hydrargyri Iodidi Rubri (½ gr.) et Potassii Iodidi (4 gr.).**

Dose.—1 twice daily.

[P2-S1] **Solvellæ Hydrargyri Iodidi (B.P.C.)** contain 8½ gr. of mercuric iodide with sufficient potassium iodide, and eosin to tint; one dissolved in a pint of water gives a 1 in 1000 solution of mercuric iodide. The red colour of the eosin rapidly fades when solutions of these tablets are exposed to bright sunlight; solutions should not, therefore, be exposed to daylight for any length of time.

**[P2] Sirop d'Iodure Mercurique (Fr. Cx.). Syn. GIBERT'S SYRUP.**

Mercuric iodide 0.5 g., potassium iodide 25 g., water 24.5 g., simple syrup 950 g.

**[P2-S1] Unguentum Hydrargyri Iodidi Rubri (B.P.C.). 1 in 25.**

For tinea may be applied to small spots, but not to large surfaces. Too strong for general use on the skin. Exophthalmic goitre has been treated by daily use of this ointment half strength.

PARENCHYMATOUS GOITRE treated by dilute mercuric iodide ointment locally. Improvement in patient's general condition and comfort.

**[P1] Unguentum Hydrargyri et Potassii Iodidi.**

Mercuric iodide 1, potassium iodide 1, water 13, lard 35, hydrous wool fat 50.

**[P1] Wool, Mercuric Iodide. ½%.**

Impregnate absorbent wool 400 under pressure with a solution of mercuric iodide 1 and potassium iodide 1, and spread out to dry.

**[P1-S1] Hydrargyri et Potassii Iodidum.  $HgI_2, KI, 1\frac{1}{2}H_2O = 647.5$ .**

A compound of this composition is obtained by crystallisation from the filtrate obtained on removing mercuric iodide formed by mixing solutions of mercuric chloride and potassium iodide. It is soluble 1 in 1 of alcohol 90%, 1 in 1 of ether and 1 in 2 of glacial acetic acid. It is not soluble in water except in presence of more potassium iodide. It is used for the same purposes as mercuric iodide.

**Hydrargyri Iodidum Viride (B.P.C.).** *Syn.* GREEN MERCUROS IODIDE, MERCURY PROTOIODIDE.

*Dose.*— $\frac{1}{4}$  to 1 grain (0.01 to 0.06 g.) gradually increased to 3 grains. Pills contain  $\frac{1}{4}$  and  $\frac{1}{2}$ ,  $\frac{1}{4}$  and  $\frac{1}{2}$  grain, and tablets contain  $\frac{1}{4}$  grain—with opium and pepper to prevent looseness of bowels.

*Incompatible* with other iodides.

A yellowish-green, odourless, tasteless powder containing mercurous iodide with free mercury. It should be kept from light, otherwise the mercurous iodide decomposes. Employed in syphilis.

[P1-81] **Hydrargyri Nitras (P. Helv. V).** *Syn.* MERCUROS NITRATE.  $\text{Hg}_2(\text{NO}_3)_2, 2\text{H}_2\text{O} = 561.3$ .

In colourless monoclinic crystals, generally damp (from adhering acid) and soluble in water, or yellow tinted (from basic salt), then not perfectly soluble in water. Used in syphilitic sores, 1 in 30 or more, as a lotion or ointment, and occasionally internally in same dose as mercuric chloride.

[P1-81] **Liquor Hydrargyri Nitratis Acidus (B.P.C.).**

Contains the equivalent of 33 $\frac{1}{3}$ % w/w of Hg dissolved in nitric acid.

Used as a caustic for syphilitic warts, and lupus.

Diluted 1 in 1000, or more, is used as a urethral injection in gonorrhœa and as a gargle for syphilitic sore throat.

An intractable and extensive case of destructive facial lupus in a boy of 11 cured by painting the lesions on three occasions. Local reaction purulent and violent but no diarrhœa and no mercurial poisoning.—W. J. O'Donovan, *Brit. J. Dermat.*, 1935, 353.

[P1] **Nebula Hydrargyri Nitratis (T.H.).** Strong ointment of mercuric nitrate 40 gr., yellow soft paraffin 40 gr., olive oil  $\frac{1}{2}$  oz., liquid paraffin to 1 oz.

[P1] **Pigmentum Hydrargyri Nitratis (B.P.C.).** *Syn.* GUTTÆ HYDRARGYRI NITRATIS.

Dilute mercuric nitrate ointment 1 in 16 in arachis oil.

*L.H.* has strong ointment of mercuric nitrate 60 gr., wool fat 30 gr., olive oil  $\frac{1}{2}$  oz., liquid paraffin to 1 oz.

[P1] **Pigmentum Hydrargyri Nitratis cum Menthole (B.P.C.)** resembles the preceding paint, but contains 1% w/v of menthol.

[P1] **"Nasal Oil" (St. M.H.)** is dilute mercuric nitrate ointment 20 gr., menthol 2 gr., lavender oil 5 m., olive oil to 1 oz.

[P1] **Oil pro Naso (P.M.H.).** *Syn.* NASAL OIL. Dilute ointment of mercuric nitrate 30 gr., menthol 5 gr., olive oil to 1 oz.

[P1] **Unguentum Hydrargyri Nitratis Forte (B.P.).** *Syn.* CITRINE OINTMENT, MERCURIC NITRATE OINTMENT, UNG. HYDRARGYRI NITRATIS, STRONG OINTMENT OF MERCURIC NITRATE.

Prepared by dissolving mercury in concentrated nitric acid in the cold, and adding the solution to a mixture of lard and olive oil heated to 150°, the heating being continued above 90° until frothing ceases. Contains about 1 of mercury in 15 of the finished ointment.

*B.P. Add. III* allows the use of arachis oil, in place of olive oil, in making strong ointment of mercuric nitrate.

Antiseptic and stimulant. Was formerly much employed in parasitic skin diseases, e.g., impetigo, sycosis, ringworm, etc.

The following formula is suggested to overcome the disadvantage of the usual preparation:—Mercuric nitrate 11.34 g., nitric acid 1.35 g., distilled water 32.31 g., white wax 5 g., cholesterol 1.5 g., white soft paraffin 48.5 g. Mix the mercuric nitrate with 1 ml. of water in a mortar, add the nitric acid and stir until dissolved. Add the remainder of the water slowly with constant stirring. Melt the soft paraffin, cholesterol (in fine powder) and white wax, and heat to 80° until the cholesterol is dissolved. Stir the mixture until it congeals. Slowly

incorporate the solution of mercuric nitrate into the base with constant trituration. Avoid contact with metal instruments. When first prepared the ointment is white, but gradually assumes a permanent light yellow colour.—Kuever and Burnside, per *Pharm. J.*, i/1940, 41.

### **Unguentum Hydrargyri Nitratis Dilutum (B.P.).**

Contains 20% of strong ointment of mercuric nitrate with yellow soft paraffin.

In tinea tarsi of great value, employed with a brush to the eyelids, also in chronic eczema, psoriasis and herpes preputialis. In pustular eczema, after removing crusts, this checks further infection; Lassar's paste and soothing lotions may then be used.

**Unguentum Hydrargyri Nitratis Dilutum (R.L.O.H.).** Strong ointment of mercuric nitrate 40 gr., yellow soft paraffin to 1 oz.

### **[P1] Unguentum Hydrargyri, Plumbi et Zinci (B.P.C.).**

*Syn.* UNGUENTUM METALLORUM.

Equal parts of strong ointment of mercuric nitrate, ointment of lead subacetate and ointment of zinc oxide.

*K.C.H.* is same as *B.P.C.* except for lead acetate ointment instead of lead subacetate ointment. *M.H.* is same as *B.P.C.* except for dilute mercuric nitrate ointment instead of strong. *W.H.* has equal parts of dilute mercuric nitrate ointment, lead acetate ointment and ointment of zinc oxide. *L.S.H.* and *St. J.H.* have mercurous chloride 10 gr., zinc oxide 20 gr., lead acetate 10 gr., strong ointment of mercuric nitrate 10 gr., benzoinated lard to 480 gr.

**Unguentum Hydrargyri cum Plumbo (St.M.H.)** contains lead acetate 10 gr., mercurous chloride 10 gr., zinc oxide 24 gr., strong mercuric nitrate ointment 24 gr., olive oil *q.s.*, lard to 480 gr.

**Ung. Metallorum (P.M.H.).** *Syn.* COMPOUND LEAD AND MERCURY OINTMENT.

Calomel 5 gr., strong solution of lead acetate 10 m., ichthammol 10 gr., strong ointment of mercuric nitrate 10 gr., soft paraffin to 1 oz.

**[P2-81] Phenylmercuric Nitrate.** *Prop. Name.* MERFENIL (*Pharmaceutical Specialities (May & Baker) Ltd., London.*)

An almost white basic salt,  $C_6H_5HgOH, C_6H_5HgNO_3$ , melting at about 180° with decomposition.

Sparingly *soluble* in water, alcohol and glycerin; more soluble in diethylene glycol.

It may be obtained by adding a solution of nitrogen tetroxide in ice-cold chloroform to an ice-cold solution of diphenylmercury in chloroform. After standing overnight at 0° the product is filtered. The precipitate is recrystallised from moist alcohol.

**Uses.** As a germicide and fungicide with low toxicity and only slightly less active in presence of body fluids. It is claimed to be 78 times as active as mercuric chloride against gram-positive cocci, and 64 times as active against fungi. 1 in 3000 for skin disinfection, 1 in 1500 for wounds, fistulae, etc., 1 in 1000 for mycotic infections, and 1 in 30,000 as vaginal douche.

Clinical studies indicate that this preparation is of great utility in the treatment of a wide variety of infections due to bacteria and fungi. Infections with the protozoon *T. vaginalis* also yield to basic phenylmercuric nitrate. It is used in the form of an aqueous 1 in 1500 solution. That given to the patient

for dilution in the preparation of a douche is a 1% solution in diethylene glycol, a drachm to a quart of warm water making approximately a 1 in 25,000 solution.—L. H. Biskind, *Lancet*, ii/1935, 1049.

**TINEA AND EPIDERMOPHYTOSIS.** Affected parts thoroughly cleansed with soap and water and a soft brush, and a 1 in 1500 ointment in a hydrophilic base containing cholesterol derivatives, gently rubbed in night and morning (over-treatment must be avoided). 205 out of 265 cases cured.—B. Levine, *J. Amer. med. Ass.*, ii/1933, 2108.

[P2-S1] **Phenylmercuric Acetate.**  $C_6H_5HgO \cdot CO \cdot CH_3 = 336.75$ .

Phenylmercuric acetate is made by heating a solution of mercuric acetate in glacial acetic acid with thiophene-free benzene. It occurs in small, white prisms, melting at  $146^\circ$  to  $147.5^\circ$ . Soluble 1 in about 600 of water; also soluble in alcohol and benzene.

Phenylmercuric acetate possesses properties and uses similar to those of phenylmercuric nitrate.

[P2] **Mersagel** (*Glaxo Laboratories, London*). Non-greasy preparation containing phenylmercuric acetate 1 in 750, in a water-soluble jelly base. Advocated for the treatment and prevention of mycotic affections of the skin.

[P2] **Volpar** (*British Drug Houses, London*). A contraceptive issued in the form of paste and gels containing phenylmercuric acetate.

[P1] **Hydrargyri Oxidum Flavum** (*B.P., Fr. Cx., P. Helv. V*).  $HgO = 216.6$ .

An orange-yellow amorphous powder obtained by interaction of mercuric chloride and sodium hydroxide.

**Insoluble** in water or alcohol 90%.

**Incompatible** with iodides and sulphides.

**Uses.** In ointments for inflamed eyelids. Should not be used whilst patient is taking iodide—violent irritation may be produced. Syphilitic sores and eczema may be treated by the 1% ointment.

[P1] **Lotio Hydrargyri Flava** (*B.P.C.*). *Syn.* YELLOW WASH.

Contains mercuric oxide precipitated from 0.5% w/v of mercuric chloride by solution of calcium hydroxide.

[P1] **Oculentum Flavum** (*B.P.C.*) contains 10% of moist yellow mercuric oxide ointment equivalent to 1% of yellow mercuric oxide.

[P1] **Oculentum Hydrargyri Oxidi** (*B.P.*) contains 1% of yellow mercuric oxide.

[P1] **Pagenstecher's Ointment** was originally prepared with a basis of spermaceti ointment. In this country yellow mercuric oxide 4% in yellow soft paraffin is usually supplied.

[P1] **Pasta Flava** (*Gt. Orn. H.*). Yellow mercuric oxide 15 gr., zinc paste to 1 oz. (Zinc paste contains starch 108 gr., zinc oxide 108 gr., simple ointment to 1 oz.).

[P1] **Unguentum Hydrargyri Oxidi Flavi** (*B.P.C.*). 2% in yellow soft paraffin. *Fr. Cx.* has 5%.

[P1] **Unguentum Hydrargyri Oxidi Flavi** (*U.S.P. XI*).

Yellow mercuric oxide 1, liquid petrolatum 1, wool fat 5, yellow wax 5, petrolatum 88.

[P1] **Unguentum Hydrargyri Oxidi Flavi** (*R.L.O.H.*) contains 2, 4 or 8 gr. of freshly precipitated mercuric oxide, pressed as free from moisture as possible, in yellow soft paraffin to 1 oz. The precipitation may be carried out as described in the *B.P.C.* for Ung. Hydrarg. Ox. Flav. Humid.

[P1] **Unguentum Hydrargyri Oxidi Flavi Humidi** (*B.P.C.*) contains 10% of freshly precipitated and very finely divided yellow mercuric oxide in a wool fat and soft paraffin basis. To be diluted for ophthalmic use as required.

[P1] **Hydrentum** (*Allen & Hanburys, London*). Neutral ointment of yellow mercuric oxide in strengths of 0.25 to 5%; also with [P1-81] atropine 0.5 and 1%. For ophthalmic use.

[P1] **Hydrargyri Oxidum Rubrum** (*B.P.C., Fr. Cx., P. Helv. V*). *Syn.* RED PRECIPITATE.  $\text{HgO} = 216.6$ .

*Dose.*— $\frac{1}{4}$  to  $\frac{1}{2}$  grain (0.004 to 0.016 g.).

A red crystalline powder obtained by heating mercurous nitrate; chemically it is identical with the yellow oxide.

[P1] **Unguentum Hydrargyri Oxidi Rubri** (*B.P.C.*). *Syn.* RED PRECIPITATE OINTMENT. 1 in 10.

For use in chronic skin affections.

[P1] **Pommade à l'Oxyde Mercurique Rouge** (*Fr. Cx.*). Red mercuric oxide 5%, in yellow soft paraffin.

[P1] **Hydrargyri Oxycyanidum** (*B.P., P. Helv. V, P. Dan.*).  $\text{HgO}, 3\text{Hg}(\text{CN})_2 = 974.5$ .

*Dose.*—By intramuscular injection,  $\frac{1}{8}$  to  $\frac{1}{4}$  grain (0.005 to 0.01 g.); by intravenous injection,  $\frac{1}{4}$  grain (0.01 g.).  $\frac{1}{8}$  to  $\frac{1}{4}$  grain (0.004 to 0.01 g.) may be given orally.

**CHEMICAL COMPOSITION.** Contains the equivalent of about 21% of  $\text{HgO}$  and 78% of  $\text{Hg}(\text{CN})_2$ . It is a mixture of approximately 34% of mercury oxycyanide and 66% of mercury cyanide. The true oxycyanide is liable to explode on heating.

The *B.P.* standards differ from those of most other European pharmacopœias, and it has been recommended that the chemical formula should be deleted from the *B.P.* monograph and the standards altered to 14.5 to 16.5% of  $\text{HgO}$  and 83.5 to 85.5% of  $\text{Hg}(\text{CN})_2$ . The official substance would then be approximately equivalent to that required by *Fr. Cx., P.G. VI, P. Ned. V Supp. II, P. Jap. V*, etc.

**Soluble** 1 in about 18 of water. The solubility varies with the proportion of  $\text{HgO}$  present.

**Uses.** It is stated to have greater antiseptic power than mercuric chloride, and to be less irritant, since it does not precipitate albumin. It is widely used in France in the treatment of syphilis, usually by the intravenous route.

In the treatment of syphilis during first week 0.05 g. in pill *per diem* as an average has been given—to be taken when the stomach is full. Should not be used with potassium iodide.

As a wound lotion 0.2 to 0.6% solutions have been employed, 1 in 10,000 to 1 in 5000 as bladder irrigant, in eye work 1 in 5000 to 1 in 1000, and 1 in 200 for instruments, which it is said not to attack. Gonorrhœa has been treated by irrigation with a 1 in 2000 solution.

[P1] **Lotio Hydrargyri Oxycyanidi** (*R.L.O.H.*).  $\frac{1}{2}$ ,  $\frac{1}{8}$  or  $\frac{1}{16}$  gr. in water 1 oz.

Hypopyon ulcers treated by subconjunctival injections.—T. L. de Courcy, *Brit. med. J.*, ii/1921, 737. Cf. *Injectio Hydrargyri Cyanidi*.

[P1] **Lotio Hydrargyri Oxycyanidi cum Zinci Sulphate** (*R.L.O.H.*).

Mercuric oxycyanide  $\frac{1}{2}$  gr., zinc sulphate  $\frac{1}{2}$  gr., water to 1 oz.

[P1] **Pasta Hydrargyri Oxycyanidi** (*L.H.*).

Mercuric oxycyanide 24 gr., tragacanth 192 gr., glycerin 4 oz., distilled water to 20 oz. Sterilise.

[P1] **Solvellæ Hydrargyri Oxycyanidi** (B.P.C.) contain 4.375 gr. of mercuric oxycyanide coloured with eosin. One dissolved in 1 pint of water gives a 1 in 2000 solution.

[P2-S1] **Hydrargyri Peptonas.** *Syn.* MERCURY PEPTONATE.

*Dose per os.*— $\frac{1}{2}$  grain (0.03 g.) increased with caution; hypodermically  $\frac{1}{4}$  grain. A brown powder containing 10% of mercuric chloride, soluble in water.

*Fr. Cx.* 1908 gives method of manufacture of a solution.

[P2-S1] **Hydrargyri Perchloridum** (B.P., *Fr. Cx.*).

*Syn.* HYDRARGYRUM BICHLORATUM (*P. Helv. V, P. Jap. V*), HYDRARGYRI BICHLORIDUM (*U.S.P. XI*), MERCURIC CHLORIDE, HYDRARGYRI CHLORIDUM CORROSIVUM, CORROSIVE SUBLIMATE.  $\text{HgCl}_2 = 271.5$ .

*Dose.*— $\frac{1}{32}$  to  $\frac{1}{16}$  grain (0.002 to 0.004 g.), but it may be increased to  $\frac{1}{4}$  grain. *Fr. Cx.* has max. single dose  $\frac{1}{4}$  grain; max. during 24 hours  $\frac{1}{2}$  grain approximately. Intravenously  $\frac{1}{32}$  grain increased.

In heavy colourless crystalline lumps or white powder.

**Antidotes and Treatment of Mercurial Poisoning.** In addition to the references below, see p. 586.

It is rare for patients to die who have not swallowed more than 7½ grains. Gastric lavage only helpful in first 15 minutes; repeated venesections and transfusions worth while also biliary drainage and colonic irrigation.—E. R. Mintz, *per Brit. med. J. Epit.*, ii/1933, 64.

Some measure of success (only 3 deaths in 48 cases) in corrosive sublimate poisoning from a therapeutic scheme comprising gastric lavage and colonic irrigation by a 5% solution of sodium bicarbonate and an internal administration of the salt in a dosage sufficient to maintain the urine alkaline to litmus.—W. B. Porter and C. E. Simons, *Amer. J. med. Sci.*, Sept., 1934, 375.

A fatal case following the self-application to the vagina of a solution of a 7-grain tablet in a pint of warm water.—B. Russell, *Brit. med. J.*, i/1934, 756.

Acute mercurial poisoning following the insertion into the vagina of two tablets containing mercuric chloride. Recovery following sodium formaldehyde sulfoxylate intravenously, together with repeated washings of the stomach and rectum, and vaginal douches with the same solution. The toxicity of mercuric chloride when used as a vaginal douche appears to be very great, especially when the mucosa is not intact.—I. M. Rabinowitch, *Canad. med. Ass. J.*, ii/1938, 429.

Acute mercury poisoning following inunction with an ointment containing 1 part in 3 of mercuric chloride successfully treated with sodium formaldehyde sulfoxylate, 10 g. in 10% solution being given intravenously daily for three days.—J. Barnes, *Lancet*, i/1939, 89.

**Soluble** 1 in 18 of water, 1 in 4 of alcohol 90%, 1 in about 14 of ether, 1 in 13 of glycerin. More soluble double salts are formed in solution with sodium, ammonium and other chlorides. These solutions contain fewer mercuric ions and are hence less poisonous (taking same weights of mercury) than  $\text{HgCl}_2$ . They are not more antiseptic.

**Incompatibles.** It precipitates most alkaloids from solutions and should therefore not be ordered with them. Interaction also occurs with alkalis and their salts and with the salts of silver and lead. Steel surgical instruments should not be dipped in this solution. It forms insoluble compounds with albuminous fluids, and is also incompatible with bodies containing tannin, soap, iodine and potassium iodide.

**Uses.** As antiseptic, but is precipitated by proteins. For the skin and for general use, a 1 in 1000 solution is used. The antiseptic action is more marked if alcohol 70% is used as the solvent.



For irrigation of wounds and for fistulæ 1 in 10,000, and for vaginal douches 1 in 100,000, but stronger solutions are frequently used. In eye lotions and in mouth-washes for glossitis and syphilitic ulceration 1 in 10,000 to 5000 may be used. Urethral injections in gonorrhœa may contain 1 in 4000. The 1 in 1000 solution with hydrochloric acid 2 in 1000 is often effective in prickly heat.

Solutions have a corrosive action on metallic instruments and cause rubber to deteriorate. Concentrations of 1 to 5% are irritant to the intact skin and may cause vesication, and absorption through the skin may cause systemic poisoning.

Internally, the perchloride has been given in syphilis. It has also been employed by intravenous injection in the form of a 1% solution (using a glass syringe and platinum-iridium needle) in syphilis, septicæmia, and acute bacterial infections. Intramuscularly its use is too painful.

**CATARACT OPERATION.** By washing the eyes with mercuric chloride 1 in 6000 before and after cocaine anesthesia, sepsis is abolished.—E. R. Shetti, *Brit. med. J.*, ii/1930, 1098.

**EMPHYEMA, PNEUMOCOCCAL.** Irrigation of the pleural cavity with 1 in 40,000 mercuric chloride, in treatment. (1 in 20,000 kills the pneumococcus in 2 hours—Choyce's *Surgery*).—F. J. Hathaway, *Brit. med. J.*, i/1925, 632.

**GUINEA WORM.** Emily, a French naval surgeon, succeeded in killing the parasite by injecting mercuric chloride solution 1 in 1000 into the body of the worm.

**OPHTHALMIA NEONATORUM.** Dangerous in treatment of (especially in conjunction with silver nitrate drops)—4 recent cases quoted. Frequent washing out with normal saline or saturated boric acid solution safe and effective.—D. Forbes, *Lancet*, ii/1931, 1102.

**SUPPURATIVE OTITIS MEDIA.** Mercuric chloride in glycerin 1 in 1000 successful where all other treatments have failed. Phenol in glycerin equally good.—T. P. Lowe, *Lancet*, ii/1928, 256.

[P2] **Carbasus Hydrargyri Perchloridi (B.P.C.).** *Syn.* **SUBLIMATE GAUZE.** Contains about 0.1% of mercuric chloride when fresh, but the strength is very variable.

[P2] **Lint, Absorbent Wool or Wood Wool,** may also be impregnated with  $\frac{1}{2}$ % each of corrosive sublimate and glycerin.

[P2] **P. Jap. V** uses mercuric chloride 2, potassium fuchsine 2, water 1500, wool 1000, i.e., 0.2%. Faintly coloured with scarlet or fuchsin "S."

[P2] **Collyrium Hydrargyri Perchloridi (B.P.C.).** 0.02% w/v.

[P2] **Collyrium Hydrargyri Perchloridi (N.I.F.).**

Mercuric chloride solution 1, distilled water to 3. For use dilute with equal quantity of hot water: strength when diluted 1 in 6000.

[P1] **Mackenzie's Eye Wash.**

Mercuric chloride 1, ammonium chloride 6, extract of belladonna 10, cochineal  $1\frac{1}{2}$ , proof spirit 55; rub together and add water to 330. Mix with equal parts of boiling water to bathe the eyes. *Caution.*—This is about five times as strong as usually employed.

[P2] **Collyr. Acid. Boric c. Hydrarg. Perchlor.** (N.I.F.). Solution of mercuric chloride:  $1\frac{1}{2}$  oz., boric acid 75 gr., distilled water to 6 oz.

For use dilute with an equal quantity of hot water.

[P2] **Gargarisma Hydrargyri Perchloridi** (1 in 1750). Mercuric chloride  $\frac{1}{2}$  gr., hydrochloric acid 1 m., glycerin 30 m., water to 1 oz.

For influenza, sore throat, especially quinsy, solution of mercuric chloride 1, acid infusion of rose petals 1. 1 tablespoonful in a teacupful of hot water as a gargle.

[P2] **Gargarisma Hydrargyri Perchloridi (T.H.).** Mercuric chloride  $\frac{1}{16}$  gr., glycerin 24 m., water to 1 oz.

[P2-81] **Glycerinum Hydrargyri Perchloridi (R.L.O.H.).**

Mercuric chloride 4, 8 or 16 gr., glycerin to 1 oz. [P2] *U.C.H.* has 0.1%. *L.H.* uses mercuric chloride  $17\frac{1}{2}$  gr., water 6 dr., glycerin to 2 pints, tinted blue. To be distinguished from the following:—

[P2-81] **Glycerinum Hydrargyri Perchloridi Alcoholicum (U.C.H.).** *Syn.* GLYCERIN-ALCOHOL-PERCHLORIDE. Mercuric chloride 35, glycerin 50, methyl blue 0.05, methylated spirit to 100. For disinfecting urine 1 dr. to a pint.

[P2] **Injectio Hydrargyri Perchloridi (Intravenous) (Gt. Orm. H.).** contains  $\frac{1}{10}$  gr. (0.0015 g.) in normal saline 85 m. (5 ml.) for children under 2 years. For older children  $\frac{1}{10}$  gr. (0.002 g.) in the same volume. May be repeated on three successive days.

[P2] **Liquor Hydrargyri Perchloridi (B.P.).** *Syn.* VAN SWIETEN'S SOLUTION (*Fr. Cx.*). 1 in 1000,  $\frac{1}{16}$  gr. in 1 drachm approx.

*Dose.*— $\frac{1}{2}$  to 1 drachm.

[P2] **Harrington's Solution.**

Mercuric chloride 0.08, alcohol 90% 64, hydrochloric acid 6, water 30 parts. For pre-operative preparation of the skin.

[P2] **Liquor Hydrargyri Perchloridi Acidus (St. T. H.).** *Syn.* TYPHOID SOLUTION. Mercuric chloride 1 oz., hydrochloric acid (strong) 25 oz., water to 500 oz. Used only as disinfectant for excreta.

[P2] **Lotio Hydrargyri Acetica.**

Mercuric chloride 1, acetic acid 75, glycerin 75, alcohol (90%) 250, rose water 500. To destroy pediculi and detach their ova.

[P2] **Lotio Hydrargyri cum Acido Carbólico (P.E.H.C.).**

Solution of mercuric chloride 20 m., dilute acetic acid 40 m., oil of turpentine 2 dr., solution of phenol (1 in 40) to 1 oz. For pediculi.

[P2] **Lotio Hydrargyri cum Oleo Terebinthinæ (U.C.H.).**

Mercuric chloride 0.6, industrial methylated spirit 12.50, oil of turpentine to 100.

[P2] **Lotio Hydrargyri Perchloridi (U.C.H.).** Mercuric chloride 0.2% coloured with turquoise blue. *St. T. H.* is the same, coloured with methylene blue. *L.H.* (coloured with turquoise blue) and *C.H.W.* are 1 in 1000. *R.L.O.H.*  $\frac{1}{8}$  or  $\frac{1}{16}$  grain in 1 ounce. The last two are not coloured. *W.H.* has  $\frac{1}{2}$  gr. in 1 oz. with 15 m. of glycerin.

[P2] **Lotio Parasitica (St. M. H.).**

Mercuric chloride  $\frac{1}{2}$  gr., acetic acid 2 dr., water to 1 oz.

[P2] **Mistura Hydrargyri Perchloridi (Gt. Orm. H.).** (Dose for 1-year-old child.)

Solution of mercuric chloride 5 m., glycerin 5 m., water to 1 dr. For infective diarrhoea of infants, in conjunction with small (5 m.) doses of castor oil.

[P2] **Mist. Hydrarg. Perchlor. (N.I.F.).**

Solution of mercuric chloride 1 dr., concentrated infusion of calumba 30 m., water to  $\frac{1}{2}$  oz.

[P2] **Mist. Hydrarg. et Pot. Iod. (N.I.F.).**

Solution of mercuric chloride 1 dr., potassium iodide 5 gr., concentrated infusion of calumba 30 m., water to  $\frac{1}{2}$  oz.

[P2-81] **Pigmentum contra Tineam.**

Mercuric chloride 1, salicylic acid 9, phenol 10, glycerin 80. Efficient in ringworm.

[P2-81] **Pigmentum Hydrargyri Perchloridi (T.H.).**

Mercuric chloride 1, glycerin 25, water 75. A potent solution to be used with very great caution and by the surgeon only. Not more than one application to be made.

[P1-81] **Pilules de Chlorure Mercurique Opiacées (Fr. Cx.).** DUPUYTREN'S PILLS.

Mercuric chloride 1, extract of opium 2, extract of agropyrum 2, powdered liquorice q.s. For 100 pills. Each pill contains mercuric chloride 0.01 g. and extract of opium 0.02 g. (*Exempt [D]*).

[P2-81] **Solvellæ Hydrargyri Perchloridi (B.P.C.)** contain  $8\frac{1}{2}$  gr. of mercuric chloride with sodium chloride, and methylene blue to colour. One dissolved in 1 pint of water gives a 1 in 1000 solution.

[P2-81] **Toxitaellæ Hydrargyri Bichloridi Magnæ (U.S.P. XI).** *Syn.* LARGE POISON TABLETS OF MERCURY BICHLORIDE, LARGE CORROSIVE SUBLIMATE TABLETS.

They contain 0.42 to 0.52 g. of  $\text{HgCl}_2$  in each tablet, and must be of a distinctive colour and not discoid in shape; the *U.S.P. XI* requires that when sold for household use they must be packed in glass bottles of distinctive angular shape with irregular or roughened sides or edges, with a red label marked "POISON" and the weight of  $\text{HgCl}_2$  in each tablet stated thereon.

[P2-81] **Toxitaellæ Hydrargyri Bichloridi Parvæ (U.S.P. XI).** *SMALL POISON TABLETS OF MERCURY BICHLORIDE.*

They contain about 0.125 g. of  $\text{HgCl}_2$ , and must be prepared and packed as described above (see *Toxitaellæ Hydrargyri Bichloridi Magnæ, U.S.P.*).

[P2] **Unguentum Desinficiens (NEISSER-SIEBERT) (P. Svec. X).** Triturate tragacanth 20 g. and wheat starch 40 g. with glycerin 170 g. Dissolve separately gelatin 7 g. in warm water 500 ml. and add mercuric chloride 3 g. and sodium chloride 10 g. to this solution. While still warm add with stirring the tragacanth mixture. Warm on water bath until homogeneous. When cool add alcohol 90% 250 g. in small lots.

[P2-81] **Unguentum Hydrargyri Perchloridi Compositum (L.H.).**

Mercuric chloride 2 gr., phenol 20 gr., glycerin 10 m., olive oil 40 m., zinc ointment to 1 oz.

[P2-81] **Sublamin (Schering, London).** MERCURY SULPHATE ETHYLENEDIAMINE. A non-irritating substitute for sublimate; superior in penetration because of absence of albumin precipitation. Supplied in 15-grain tablets.

[P1] **Sal Alembroth.** *Syn.* AMMONIO-MERCURIC CHLORIDE.

$(\text{NH}_4)_2\text{HgCl}_4 \cdot \text{H}_2\text{O} = 396.5$ .

A crystalline powder. Soluble 2 in 1 of water, 1 in 4 of alcohol 90%, also in glycerin. Is a powerful antiseptic, but does not combine with albumin quickly and hence is not very irritating.

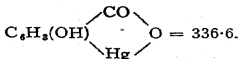
**Uses.** Formerly used for [P1] medicating dressings, bandages, gauze, wool gauze, and wool tissue, 1 or 2% (which are dyed blue), also as an intramuscular injection for syphilis. (*Dose.*—10 minims of 5% solution. Painful. Slowly eliminated.)

[P2-81] **Hydrargyri Salicylas (B.P.C., U.S.P. XI, P. Helv. V).**

**Dose.**— $\frac{1}{10}$  to  $\frac{1}{2}$  grain (0.003 to 0.02 g.). Intramuscularly,  $\frac{1}{10}$  grain in 10 minims of liquid paraffin, increased up to 1 grain. *U.S.P. XI* average dose, intramuscularly, 1 grain twice a week. *P.G. VI* gives max. single dose  $2\frac{1}{2}$  grains (0.15 g.). It is also official in *P. Ital. V*.

A white powder containing 54 to 59.6% of Hg.

When produced by the interaction of mercury oxide and salicylic acid, the chief constituent is anhydro-hydroxy-mercuric-salicylic acid of formula



Almost *insoluble* in water (but soluble in solutions of sodium hydroxide and sodium carbonate), scarcely soluble in alcohol 90%. This is the basic mercuric salicylate as distinguished from the neutral or normal salt (see below).

**Uses.** As an antiseptic and antisymphilitic and as a dusting powder or ointment for sores. It has the advantage of causing

relatively little pain when given by injection. Should not be given in large doses with potassium iodide.

As an injection for gonorrhœa 15 minims of a mucilage suspension 1-300 has been used.

**BELL'S PALSY.** Three to four injections intramuscularly in 10 to 14 days of 10 m. of 1% suspension of mercury salicylate in liquid paraffin gave excellent results.—*P. A. Harry, Prescriber, 1926, 290.*

**LOCAL SKIN AFFECTIONS** well treated with mercury salicylate in liquid paraffin injections intramuscularly, 1 gr. per ml. dose.—*W. A. Elliott, Brit. med. J., i/1925, 551.*

[P2-81] **Hydrargyri Salicylas, Neutrale.**  $(C_6H_5 \cdot OH \cdot COO)_2Hg = 474.7$ .

*Dose.*—Hypodermically  $\frac{1}{2}$  to 1 grain suspended 1 in 10 in liquid paraffin. Comparatively non-irritant.

Quinine-urea (2%) added as follows relieves pain:—

Quinine-urea 2, water 2, dissolve and mix with wool fat 20. To this add mercuric salicylate 10, liquid paraffin *q.s.* to 100.

[P2-81] **Merthiolate** (*Lilly, London*). SODIUM ETHYLMERCURITHIOSALICYLATE,  $C_6H_5 \cdot Hg \cdot S \cdot C_6H_4 \cdot COONa$ .

[S3] "*Sodium ethyl mercurithiosalicylate—in therapeutic substances containing less than 0.1% of sodium ethyl mercurithiosalicylate as a preservative.*"

Contains 49% of Hg in organic combination. A potent germicide for sterilising tissue surfaces. Readily soluble in normal saline solution or cold water. Less toxic than mercuric chloride. For general application and for sterilising instruments 1 in 1000 solution; for mucous membranes 1 in 5000 to 1 in 2000; for ophthalmic use 1 in 5000; for bladder irrigation 1 in 10,000 to 1 in 5000.

[P2] **Merthiolate Cream.** Contains Merthiolate 1 in 1000 incorporated in a vanishing cream basis made by emulsifying stearic acid and lanolin with triethanolamine. For use in mycotic skin infections and in acne vulgaris and acne pustulosa.

[P2] **Merthiolate Suppositories.** 10 g. suppositories containing Merthiolate 1 in 1000 in a glycerin and gelatin base. For use in non-specific infections and inflammations of the cervix and upper vagina.

**Hydrargyri Subchloridum (B.P.).** *Syn.* MERCUROUS CHLORIDE, CALOMEL (*P. Dan.*), SUBCHLORIDE OF MERCURY, MERCURIUS DULCIS (*P. Ned. V*), HYDRARGYRI CHLORIDUM MITE (*U.S.P. XI*), HYDRARGYRUM CHLORATUM (*P. Helv. V, P. Jap. V*), PRÉCIPITÉ BLANC (*F.E. VIII*) (distinguish from British and *P. Belg. IV* white precipitate which is Hydrargyrum Ammoniatum).  $HgCl = 236.1$ .

*Dose.*— $\frac{1}{2}$  to 3 grains (0.03 to 0.2 g.); by intramuscular injection  $\frac{1}{2}$  to 1 grain (0.03 to 0.06 g.). *U.S.P. XI* average laxative dose  $2\frac{1}{2}$  grains. *Fr. Cx.* has maximum single dose 15 grains, maximum during 24 hours, 15 grains. *P. Helv. V* has approx. 3 grains and 10 grains respectively.

Heavy white powder. It can also be obtained as small, soft, scaly crystals for eye work (*see Duret's calomel, Vol. II*). *Fr. Cx.* contains Precipitated Mercurous Chloride (*syn. WHITE PRECIPITATE*), an amorphous powder, and Sublimed Mercurous Chloride (*syn. CALOMEL*) minutely crystalline.

**Insoluble** in water, ether or alcohol.

**Incompatible** with acids, alkalis (*see Lotio Nigra*), with sodium and potassium chloride and with bromides, iodides, sulphur, cherry laurel water, and phenazone.

**Uses.** Alterative, purgative and antisyphilitic. It is not suitable for long-continued use internally on account of its systemic

actions. Was always considered a cholagogue, but at the present time is thought to empty the gall-bladder only, not to increase the actual amount of bile formed. Most useful purgative for congested liver and dyspepsia generally. To be given at bed-time followed by morning saline draught. Useful where there is intestinal putrefaction, *e.g.*, in dysentery, faecal accumulation, typhoid. For torpid liver  $\frac{1}{4}$ -grain doses hourly valuable, and repeated small doses, *e.g.*,  $\frac{1}{2}$  gr. every hour for 12 to 18 hours, are of value in follicular tonsillitis and may abort a quinsy if administered before suppuration occurs. As dusting powder to ulcers and many skin diseases (but not to cornea of the eye if potassium iodide is being given). It is non-irritant and may be employed in any concentration. Applied dry it relieves pruritus ani and as an ointment relieves the pain of hæmorrhoids. Administered by intramuscular injection in syphilis, calomel is painful but highly active. Ointments containing from 25 to 33% of calomel are effective venereal prophylactics if applied within four hours of exposure.

**HÆMORRHOIDS.** In the early stages, as a palliative measure, an ointment composed of one part of calomel and seven parts of Vaseline is of value. A small amount is inserted into the anal canal overnight on retiring and in the morning after defecation. It is slightly astringent and sedative. Ointments containing strong astringents should be avoided.—Ivor Back, *Med. Pr.*, ii/1936, 203.

**Injectio Hydrargyri Subchloridi (B.P.).** *Syn.* CALOMEL INJECTION.

**Dose.**—By intramuscular injection, 10 to 20 minims (0.6 to 1.2 ml.).

Contains about 5% *w/v* of very finely powdered mercurous chloride with camphor and creosote in wool fat and olive oil. *B.P. Add. III* allows the use of arachis oil, in place of olive oil, in making injection of mercurous chloride.

Although calomel injections are highly effective they have gone largely out of use, since it is impossible to control their absorption, and they are apt to produce excessive stomatitis.

[P2] **Injectio Hydrargyri Subchloridi Hypodermica.** Lambkin's original formula.

**Dose.**—10 minims injected once a week.

Calomel 10 gr., suspended in  $\frac{1}{2}$  oz. of sterile olive oil containing 2% of phenol. Morphine  $\frac{1}{2}$  gr. may be given afterwards to relieve pain.

[P] **Gargarisma Hydrargyri et Potassii Chloratis (T.H.).**

Black wash 2 dr., gargle of potassium chlorate  $\frac{1}{2}$  oz. (gargle of potassium chlorate contains potassium chlorate 12 gr., sodium bicarbonate 6 gr., potassium bicarbonate 6 gr., water to 1 oz.).

[P1] **Lotio Hydrargyri Nigra (B.P.).** *Syn.* BLACK MERCURIAL WASH, BLACK WASH.

Contains mercurous oxide equivalent to 0.7% of mercurous chloride with glycerin and solution of calcium hydroxide.

[P1-81] **Pilulæ Hydrargyri Subchloridi Compositæ (B.P.C.),** *syn.* PLUMMER'S PILLS, *dose*—1 or 2 pills, contain mercurous chloride 1 gr., sulphurated antimony 1 gr., guaiacum resin 2 gr.

**Pil. Calomel et Menthol. (N.I.F.).** Each pill contains calomel, menthol and powdered ginger, of each  $\frac{1}{2}$  gr.

**Pilula Hydrargyri Subchloridi, Rhei, Cascaræ et Capsicini.**

Calomel  $\frac{1}{2}$  gr., extract of rhubarb 2 gr., extract of cascara 1 gr., capsicin  $\frac{1}{2}$  gr. Relieves constipation, e.g., that arising from large doses of bismuth.

**[P1-81] Pulvis Basilicus.**

*Dose.*—For a child of 2 years, 4 grains (0.25 g.); of 6 years or upwards, 8 grains (0.5 g.).

Mercurous chloride 3, scammony 3, potassium acid tartrate 3, jalap 1, ginger 1, antimonial powder 1.

**Pulvis Hydrargyri Subchloridi Compositus (St. J. H.).**

Mercurous chloride 2, boric acid 7, starch 7.

**Unguentum Hydrargyri Subchloridi (B.P.).** *Syn.* CALOMEL OINTMENT. Mercurous chloride 1, simple ointment 4. To relieve irritation.

Calomel ointment prepared with a wool fat and soft paraffin basis is less effective as an antiseptic than one prepared with soft paraffin only. The difference appears to be due to the increased viscosity caused by the incorporation of the wool fat.—L. C. Britt, *J. Amer. pharm. Ass.*, 1937, 646.

**IMPROVED OINTMENT.** A suspension of calomel in gelatin is obtained by adding 3% mercurous nitrate to an equal volume of 2% gelatin, containing 1.2% sodium chloride, washing by dialysis and concentrating to contain 1 g. calomel in 3 g. of suspension. Incorporation in an ointment base gave a product of higher antiseptic value than the usual preparations.—*J. Amer. pharm. Ass.*, 1937, 26, 1241.

**[P1] Unguentum Hydrargyri Subchloridi Compositum (B.P.C.).** *Syn.* CALOMEL CREAM, PROPHYLACTIC OINTMENT.

Mercurous chloride 25%, and mercuric oxycyanide 0.075%, in a wool fat and paraffin basis. As a prophylactic measure against syphilis. "Preventive Capsules" (*P.M.H.*) contain 36 gr. of an ointment of similar composition.

Suspicious cracks or hangnails should have this ointment well rubbed in:—Calomel 33, soft paraffin 10, wool fat 57.

**[P2-81] Hydrargyri Succinimidum (U.S.P. XI).** *Syn.* IMIDO-SUCCINATE OF MERCURY.  $[C_2H_4(CO)_2N]_2Hg = 396.7$ .

*Dose.*—By injection,  $\frac{1}{4}$  to  $\frac{1}{2}$  grain (0.016 to 0.02 g.).

Mercury succinimide is a white powder, soluble in water about 1 in 28. Hypodermically in syphilis has been used in 2½% solution. Addition of cocaine nitrate diminishes pain. Compared with other salts of mercury its solutions are said to be relatively non-irritating.

**Hydrargyri Sulphidum Rubrum.** *Syn.* VERMILION, CINNABAR (*P. Jap.* 7), CHINESE RED.  $HgS = 232.7$ . Brilliant red powder insoluble in water and dilute acids prepared by subliming a mixture of mercury and sulphur. Both this and the black variety, **Hydrargyri Sulphuretum cum Sulphure** (*syn.* HYDRARGYRUM SUBSULPHIDUM NIGRUM, ETHIOP'S MINERAL), of same composition are now rarely employed therapeutically.

**Unguentum Hydrargyri Bisulphidi (L.H.).** *Syn.* UNGUENTUM CINNABAR ET SULPHURIS.

Mercuric sulphide 4 gr., precipitated sulphur 15 gr., yellow soft paraffin to 1 oz.

**[P1-81] Æthiops Antimonialis.** A mixture of equal parts of black mercuric sulphide and grey antimony sulphide.

**Hydrargyri Persulphas.** *Syn.* MERCURIC SULPHATE, HYDRARGYRI SULPHAS.  $HgSO_4 = 296.7$ .

*Dose.*—2 to 5 grains (0.12 to 0.3 g.).

A white powder made by dissolving mercury in boiling strong sulphuric acid. Water decomposes it with formation of yellow turpeth mineral, Hydrargyri Subsulphas (*Fr. Cx.*) or mercuric oxysulphate,  $HgSO_4 \cdot 2HgO = 729.9$ .

It is a prompt emetic in dose of 2 to 5 grains which was given to children in croup and diphtheria to expel false membrane. Does not produce purging. Turpeth mineral ointment, Bazin's ointment, is 1 in 30 of benzoinated lard. Used for ringworm and seborrhœa capitis.

[P2-81] **Hydrargyri Tannas** (B.P.C.).

Dose.—1 to 2 grains (0.06 to 0.12 g.), in pills or tablets, often with opium to prevent diarrhœa.

In brownish-green powder or scales containing 40 to 50% of Hg. Has been used in syphilis.

[P1-81-84] **Merbaphenum** (U.S.P. XI). Prop. Name. NOVASUROL (Bayer Products, London).

Average dose.—2½ gr. by hypodermic injection. Is usually given intravenously or intramuscularly as a 10% solution.

A double salt of sodium mercurichlorophenylxyacetate with barbitone. A white crystalline powder containing about 34% of Hg. Soluble in water giving an alkaline solution.

Uses. Causes profuse and rapid diuresis, especially in cardiac dropsy, but liable to produce toxic symptoms and superseded now by mersalyl.

[P2-81] **Mercurochromum** (B.P.C.). Syn. and Prop. Names.

MERCUROCHROME-220 SOLUBLE, DI-SODIUM DIBROMOHYDROXY-MERCURI-FLUORESCIN, MERCUCROCOL (Evans, Sons, Lescher & Webb, Liverpool), MERCUROME (Martindale, London), PLANOCHROME (Pharmaceutical Specialities (May & Baker) Ltd., London).

$C_{20}H_7O_5Br_2 \cdot HgOH \cdot Na_2 = 750.5$ .

It is patented in U.S.A. and in some other countries but not in England, and "Mercurochrome" is a trade mark in U.S.A. and some other countries, but not in England.

Dose.—By intravenous injection 0.002 to 0.005 g. per kilo, i.e., 0.13 to 0.32 g. per 10 stone (63½ kilo) man, preferably in 0.5% or greater dilution.

Iridescent green scales giving a red solution which shows a green fluorescence when dilute. It contains 25 to 28% of Hg.

The B.P.C. requires mercurochrome when used for intravenous injection to comply with a biological test to ensure that its toxicity is not greater than that of a standard sample of mercurochrome kept by the Pharmaceutical Society of Great Britain. (See Vol. II.)

**Soluble** readily in water, 1 in 185 of dehydrated alcohol, 1 in 65 of alcohol 90%. Insoluble in acetone, but soluble in a mixture of acetone and diluted alcohol. Insoluble in chloroform and ether. Solutions should not be boiled or autoclaved.

**Incompatible** with acids, alkaloidal salts, and with most local anæsthetics.

Uses. Mercurochrome has been extensively advocated as an antiseptic but most recent experiments show that, *in vitro*, its action is relatively weak. Intravenously in septicæmic conditions it is now regarded as of little value, and mercurial poisoning may result. Intravenous injections are usually followed by high temperature and vomiting, sometimes leading to prostration and collapse, and should only be employed as an emergency hospital procedure. As a vesical injection in cystitis, pyelitis, and in gonorrhœa the 1% solution is used.

As a non-irritant antiseptic for local use a solution of mercurochrome 2 in water 35, alcohol 95% 55, and acetone 10 is employed.

**BURNS.** Preferable to tannic acid (comparison of 2696 cases). It is an effective antiseptic in the presence of protein; the crust formed is thin and transparent; bed linen is not destroyed; it is non-irritant to tissues; a 2% aqueous solution is stable indefinitely; epithelisation under the scab is rapid. No general anæsthetic is given, all dead tissue is stripped off and the denuded area swabbed with normal saline and then with 2% aqueous solution of mercurochrome; the surface is then dried with an electric drier. On the first day 4 applications are given; on the second, 3; and on the third, 2. The area is dried off after each application and is always kept exposed to the atmosphere.—A. C. Turner, *Brit. med. J.*, ii/1935, 995.

**CHRONIC CERVICITIS.** Responded well when treated with a douche or paint.—L. C. Rivett, *Brit. med. J.*, ii/1930, 866.

In cervical discharges (other than gonorrhœa) apply a 10% solution to the cervix on a swab and leave in place; paint the vagina with the same solution.—Colonel L. W. Harrison, *Lancet*, i/1932, 452.

**CYSTITIS.** Intractable cystitis with frequent micturition and pyuria well treated, especially amongst women.—K. W. Heritage, *Brit. med. J.*, ii/1930, 866.

**CONJUNCTIVITIS.** Painted on both lids at once it cuts short duration. Invaluable in chronic cases. Superior to silver, is less irritating and cannot damage cornea. Two paintings a week. PARINAUD'S CONJUNCTIVITIS cleared up. Maternity Department of Bristol Royal Infirmary issues 1% solution instead of silver for the eyes of new-born babies. Decrease of ophthalmia neonatorum. CORNEAL ULCERS can be painted with benefit. BLEPHARITIS benefited by painting. In ophthalmic surgery 1% is painted over the skin of the eyelids.—E. R. Chambers, *Brit. med. J.*, ii/1930, 992.

Parinaud's conjunctivitis cleared up in 2 weeks by drops; also useful in tuberculous conjunctivitis and in chronic dacryocystitis.—J. Cole Marshall, *Brit. med. J.*, ii/1930, 1102.

**MUSTARD GAS POISONING.** Patients contaminated with mustard gas were treated with mercurochrome solution with the result that the pain was reduced and no secondary infection occurred. These experiments are not conclusive, but suggest that it would be desirable to try out the application of mercurochrome on patients when opportunity offers.—Per *Quart. J. Pharm.*, 1940, 192.

**OBSTETRICS.** Induction of labour by 0.5% mercurochrome in glycerin through a catheter into the uterus. Succeeded in about 66% cases. In uterine sepsis 1% by intrauterine injection almost invariably cures.—R. Kelson Ford, *Brit. med. J.*, ii/1930, 727.

**OTORRHOEA.** In the subacute stage a 1% solution often acts like a charm, but should not be used for more than a fortnight as it is a definite tissue poison.—E. Watson-Williams, *Brit. med. J.*, ii/1933, 49.

**POST-OPERATIVE RETENTION.** A special technique to promote post-operative voiding after operations in the region of the bladder consists of instilling into the bladder 1 ounce of 0.5% aqueous solution of mercurochrome in the operating room. The results after pelvic laparotomies have been very gratifying, the incidence of catheterisation having been reduced from 51% in a control series to 6.5% in a series of 500 cases in which this procedure was used.—J. D. Woodruff and R. W. Te Linde, *J. Amer. med. Ass.*, ii/1939, 1451.

[P2-S1] **Metaphen** (*Abbott Laboratories, London*).

The anhydride of 4-nitro-5-hydroxymercuri-o-cresol, a relatively non-irritating germicide. It is dissolved in water with the aid of sodium hydroxide which forms a sodium salt.

For use on infected areas, skin sterilisation and instruments and hands, and in wounds and open cuts; also for instillation in gonorrhœa, and in ophthalmology. Stated to be 11 times more potent than mercuric chloride. Usually employed in 1 in 5000 solution, though up to 1 in 1000 may be used.

**IMPETIGO CONTAGIOSA.** Thoroughly cleanse skin round infected area and paint the lesion with several layers of Metaphen in flexible collodion 1 : 5000 which is permitted to dry layer by layer. In 24 hours the easily removable layers are removed, the adherent part is left on and the mixture reapplied in several layers; repeat procedure on third day. On the 4th day all the Metaphen-collodion preparation is removed with the underlying incrustation. If the underlying skin is dry apply 2% ammoniated mercury ointment, but if still moist repeat the Metaphen-collodion treatment for another 3 days. Over 200 cases treated with success.—L. Hollander and J. J. Hecht, *Amer. J. Dis. Childh.*, Aug., 1934, 269.



**UNDULANT FEVER.** Prompt decline in temperature and improvement of symptoms in ten cases treated with Metaphen intravenously in doses of 10 ml. of 1 in 1000 solution, the number of injections ranging from two to thirteen. Injections were given daily for the first week and twice weekly afterwards. No toxic reactions were observed.—K. H. Abbott *et al.*, *per Prescriber*, 1938, 250.

[P2-81] **Neptal** (*Pharmaceutical Specialities (May & Baker) Ltd., London*).  $\alpha$ -Hydroxymercuripropionamidocarboxyphenoxycetic acid. A mercurial diuretic used in nephritis, oedema of cardiac or renal origin, and in pleural or pericardial effusions. It is stated to be free from toxicity in therapeutic doses, and to have rapid and prolonged action. Ampoules of 1 ml. contain 0.092 g. of active product, and suppositories contain 0.5 g. with 5% theophylline.

**Dose.**—0.8 to 1.5 ml. intramuscularly daily or every other day, or, in urgent cases, the same dose intravenously diluted to 10 ml. with normal saline.

[P2-81] **Novurit** (*Chinoin A.G., Budapest; Martindale, London*). Known in the U.S.A. as MERCURIN.

A mixture of 20% of the  $\beta$ -methoxy- $\gamma$ -hydroxy-mercuripropylamide of trimethylcyclopentanedicarboxylic acid and 80% of the sodium salt. It is a white, bitter powder, slightly soluble in water and ether, more soluble in alcohol and dilute sodium hydroxide.

Suppositories contain 0.5 g. of Novurit, ampoules contain 0.1 g. with 0.05 g. theophylline in 1 ml. **Dose.**—1 to 3 intramuscular or intravenous injections a week, commencing with a dose of 0.5 to 1 ml. and increasing to 2 ml.; suppositories, 1 or 2 a week. In cardiac oedema, ascites, hepatic cirrhosis, cardiorenal oedema.

Ten cases of congestive heart failure with oedema have been treated with this suppository and also with Novurit intravenously and with Salyrgan intravenously. The average twenty-four hours' excretion of urine per dose was for the suppository 87.2 oz., for Novurit intravenously 121.1 oz., for Salyrgan intravenously 91.8 oz. The previous administration of ammonium chloride results in an increased diuresis. With the suppositories 68.7% of the diuresis occurred within the first twelve hours, while the corresponding figure for Salyrgan intravenously was 81.7%. The diuresis does not extend beyond twenty-four hours. No toxic or irritative effects of the suppository have so far been detected. It is concluded that Novurit suppository is an effective and safe diuretic.—J. Parkinson and W. A. R. Thomson, *Lancet*, i/1936, 16.

[P2-81] **Mersalylum** (*B.P. Add. I*). *Syn. and Prop. Name.* MERCURGAN, SODIUM SALICYL-( $\gamma$ -HYDROXYMERCURI- $\beta$ -METHOXY-PROPYL)-AMIDE-O-ACETATE, SALYRGAN (*Bayer Products, London*) (available only in 10% solution for injection).  
 $(\text{HgOH})\text{CH}_2\cdot\text{CH}(\text{OCH}_3)\text{CH}_2\cdot\text{NHCO}\cdot\text{C}_6\text{H}_4\cdot\text{O}\cdot\text{CH}_2\cdot\text{COONa}$

= 505.7.

**Dose.**—No dose is given in *B.P. Add. I*, which states that for injections the official *Injectio Mersalyli* should be used.

White deliquescent powder containing 38.5 to 40.5% of Hg calculated on the dried substance.

**Soluble** 1 in 1 of water, 1 in 3 of alcohol 95%, 1 in 2 of methyl alcohol; insoluble in ether and chloroform. Aqueous solutions containing sodium chloride or other salts decompose with formation of toxic compounds except in the presence of some substance such as theophylline, which inhibits decomposition.

[P2-81] **Injectio Mersalyli** (*B.P. Add. I*).

**Dose.**—8 to 30 minims (0.5 to 2 ml.) by intramuscular or intravenous injection. The smaller dose is given to test tolerance. It is usually given intravenously.

Mersalyl 10 g., theophylline 5 g., in sterilised water to 100 ml., with sodium hydroxide *q.s.* to give a pH of about 7.8. The addition of theophylline enhances the action.

**Contraindicated** in acute disease of the kidneys and advanced nephritis, and in enterocolitis, fever, or hæmorrhagic states.

**Uses.** Chiefly used as a diuretic in ascites and œdema of cardiac and cardio-renal origin, and in ascites resulting from cirrhosis of the liver.

Intravenous route gives better and quicker response. Diuresis begins in 1 to 4 hours and is complete in 8 to 12 hours; best given in the morning. Ammonium chloride, 8 to 15 g. daily for 3 or 4 days before injection, improves response.—G. W. Collins, per *Prescriber*, 1929, 71.

Severe toxic effects from intravenous injection of doses larger than stated *antea*.—C. T. Andrews, *Lancet*, ii/1931, 132.

Found to rank second in importance to digitalis in treatment of heart failure. Not only causes diuresis but frequently a considerable diminution in frequency of attacks in cardiac asthma. No evidence of renal damage.—H. T. Hyman and N. M. Fenichel, per *Lancet*, ii/1932, 139.

Salyrgan should never be employed to start diuresis in cases of acute anuria; when renal insufficiency exists in the form of uremia, it is hazardous to use it and it is likely to increase renal insufficiency. Its use is not advised if the blood urea is greater than 50 or 75 mg. per 100 ml., or if erythrocytes are present to any degree in the urine. Salyrgan is most successful in those cases of minimal renal insufficiency, namely, œdema due to cardiac decompensation, nephrosis, polyserositis, and in the œdemas of indeterminate origin. 0.5 ml. is first given intravenously, and if no toxic effect is noted, 2 ml. may be given the following day and repeated every third or fourth day.—M. W. Binger, *Proc. Mayo Clin.*, October 7, 1936, 649.

Salyrgan given intramuscularly is useful in reducing localised œdema after injuries (e.g., following fractures), though some cases fail to respond.—M. J. Petty, *Brit. med. J.*, ii/1938, 944.

**CARDIAC ŒDEMA.** Salyrgan can be used without interruption and without fear of toxic effects. In one case a total of 270 injections was given over 5 years. Beneficial not only in relief of œdema but in staving off symptoms of early cardiac insufficiency.—I. M. Dixon, *New Engl. J. Med.*, i/1934, 800.

[P2-S1] **Dilurgen** (*Richter, London*). Oxy-mercuric-allyl-succinyl-carbamide. A mercurial diuretic with a mercury content of 44 to 46%. Ampoules of 1 ml. contain 0.1 g. of Dilurgen and 0.043 g. of theophylline. *Dose*.—1 or 2 ml. intramuscularly daily or every other day. Also supplied in the form of suppositories containing 0.5 g. of Dilurgen Sodium.

[P2-S1] **Esidrone** (*Ciba, Horsham*). The sodium salt of pyridinedicarboxy- $\beta$ -mercuri- $\omega$ -hydroxypropylamidetheophylline, containing 31.2% mercury in a non-ionisable form and 28% theophylline chemically combined. *Dose*.—One ampoule of 1.1 ml. intravenously or intramuscularly two or three times weekly. A diuretic for use in cardiac œdema, dropsy, ascites and for reduction of obesity. The action is enhanced by previous acidification of the organism with ammonium chloride. The mercury is rapidly eliminated.

## HYDRASTIS

*B.P.C., Fr. Cx., P. Jap. V, P. Helv. V.*

*Syn. GOLDEN SEAL, YELLOW ROOT.*

*Dose*.—10 to 30 grains (0.6 to 2 g.).

The dried rhizome and rootlets of *Hydrastis canadensis* (Ranunculaceæ). *Fr. Cx.* and *P. Helv. V* require 2.5% of hydrastine.

**Uses.** Internally, it exerts an astringent and tonic action in congestion and chronic inflammation of the mucous membranes of the respiratory and genito-urinary tracts, and is of value in

catarrhal affections of the nose and throat and in chronic catarrhal gastritis and enteritis. The drug and its alkaloids cause uterine contraction and are used in menorrhagia and dysmenorrhœa.

Externally, it is of value in chronic inflammation of the mucous membrane, also for cracks and fissures of the nipple. It stimulates indolent ulcers, and as a lotion (1 in 20 of liquid extract) checks profuse sweating. In gonorrhœa, an injection of a 1% solution of the liquid extract has been employed. It is also used, in the form of suppositories or ointment, in the treatment of hæmorrhoids.

### **Extractum Hydrastis Liquidum (B.P.C.).**

*Dose.*—5 to 15 minims (0.3 to 1 ml.) Contains 2% of hydrastine. Large doses, 30 m. twice daily, have been given with success in chronic constipation with hypochlorhydria. A preparation containing 1.5% of hydrastine has been recommended as a more practical proposition.

### **Extractum Hydrastis (B.P.C.). Syn. HYDRASTIN.**

*Dose.*— $\frac{1}{2}$  to 2 grains (0.03 to 0.12 g.). A dry alcoholic extract containing 8% of hydrastine. It is sometimes difficult to prepare an extract of this strength, and a standard of 5% of hydrastine has been recommended.

Aperient, cholagogue, stomachic, and tonic; 3 to 6 grains in a pill, followed by effervescing sodium sulphate, is a useful biliary stimulant.

### **[P1-81] Mistura Hydrastis et Ergotæ.**

Liquid extracts of hydrastis and ergot of each 30 m., chloroform water to 1 oz. for a dose.

Stated to be a potent remedy in menorrhagia.

### **Tinctura Hydrastis (B.P.C.).**

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Prepared with 10% of the liquid extract in alcohol 60%.

*Fr. Cx.* requires not less than 0.4% of alkaloids.

**Liquor Sedans (Parke, Davis, London).** *Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

A specialty stated to contain in 1 oz. hydrastine representing fluid extract of hydrastis 30 m., black haw (*Viburnum prunifolium*) 60 gr., Jamaica dogwood (*Piscidia piscipula*) 30 gr., with aromatics.

As ovarian and uterine sedative; for dysmenorrhœa, threatened miscarriage, etc.

**Hydrastina.**  $C_{21}H_{21}O_6N = 383.2$ .

*Dose.*— $\frac{1}{2}$  to 1 grain (0.016 to 0.06 g.).

An alkaloid in white prismatic crystals, slightly soluble in water, but soluble 1 in 120 of alcohol 90%, 1 in 2 of chloroform and 1 in 83 of ether; taste very bitter. ~~May~~ be distinguished from extract of hydrastis, sometimes called hydrastin.

**Hydrastine Hydrochloridum (B.P.C.).**  $C_{21}H_{21}O_6N.HCl = 419.6$ .

*Dose.*— $\frac{1}{2}$  to 1 grain (0.016 to 0.06 g.) orally, or hypodermically as a 10% solution.

A crystalline soluble salt, constricts peripheral vessels and said to cause uterine contraction and arrest hæmorrhage.

**Hydrastinina (Fr. Cx.).**  $C_{11}H_{13}O_5N$ . *Dose.*— $\frac{1}{2}$  to  $\frac{1}{4}$  grain (0.016 to 0.03 g.) increased up to 1 grain (0.06 g.). *Fr. Cx.* gives max. single dose 0.05 g.; max. in 24 hours 0.15 g.

Is obtained by the oxidation of hydrastine. In white or faintly yellow crystals soluble in alcohol, ether and chloroform, moderately soluble in hot water.

**Hydrastininæ Hydrochloridum** (B.P.C., Fr. Cx., P. Ital. V, P.G. VI, P. Helv., P. Dan., P. Belg. IV).

$C_{11}H_{15}O_2NCI = 225.6$ .

**Dose.**— $\frac{1}{4}$  to  $\frac{1}{2}$  grain (0.016 to 0.03 g.) hypodermically. Orally the dose may be increased up to 1 grain (0.06 g.). Fr. Cx. has max. single dose  $\frac{3}{4}$  grain; max. during 24 hours  $2\frac{1}{2}$  grains approx.

In pale citron yellow crystals, soluble 1 in 1 of water. Has been used for internal hæmorrhage hypodermically.

Useful in menorrhagia and dysmenorrhœa.

**Beberinæ Sulphas** (B.P.C.). Syn. BEBERINE, BUXINE or PELOSINE SULPHATE. **Dose.**—1 to 5 grains (0.06 to 0.3 g.).

A mixture of alkaloidal sulphates with various impurities obtained from nectandra (bebeeru) bark, the stem bark of *Nectandra Rodiei* (Lauraceæ). It occurs in bitter translucent scales containing about 30% of beberine. Soluble 1 in about 1 of water; sparingly soluble in alcohol. Antipyretic and tonic similar to quinine, useful in menorrhagia.

Beberine Hydrochloride is also occasionally used. In reddish-brown scales.

**Berberidis Cortex** (B.P.C.). Barberry bark is the dried bark of the stem of *B. vulgaris*, and has been administered as Tinctura Berberidis Corticis (1 in 10), dose— $\frac{1}{2}$  to 1 drachm, or as a decoction (1 in 20) or infusion (1 in 20).

**Berberinæ Sulphas** (B.P.C.). Syn. BERBERINE (or BERBERINIUM) ACID SULPHATE.  $C_{20}H_{18}O_4N(HSO_4) = 433.2$ .

**Dose.**—1 to 5 grains (0.06 to 0.3 g.).

The acid sulphate of berberine, an alkaloid present in hydrastis and calumba but obtained mainly from *B. vulgaris*. In bright yellow acicular crystals or as a dark yellow powder with bitter taste.

**Soluble** 1 in 150 of water and in alcohol (90%).

**Uses.** Has been given for indigestion, diarrhœa, malaria, and sickness in pregnancy. Is administered by injection in oriental sore.

Berberine sulphate in water said to be effective in oriental sore. Inject into the sore, and repeat after a week.—R. L. Varma, *Indian med. Gaz.*, 1927, 62, 84.  $\frac{1}{4}$  grain of the sulphate in 1.5 ml. of water. Hypertonic and isotonic saline strongly recommended in conjunction. Better than tartar emetic intravenously.—P. V. Karamchandani, *Lancet*, i/1930, 78.

Successful treatment of oriental sore with 3 ml. of 2% berberine acid sulphate. Two to four injections effected a cure in 6 cases.—*Prescriber*, 1931, 355.

Berberine acid sulphate is of undoubted value in cutaneous leishmaniasis. 1 or 2 ml. of a 1 per cent. aqueous solution is infiltrated by means of a fine needle into the margins of the lesion. Four or five punctures are made and the infiltration is evenly spread. The injections are given once a week, the part being kept covered. Three treatments is frequently sufficient; occasionally a large number is necessary.—R. N. Chopra, B. B. Didshit, and J. G. Chowlan, *Indian med. Gaz.*, 1932, 194.

Analysis of treatment of over 300 cases. All those who received 15 or more injections (132) were definitely cured. If persevered with, the injections are a certain cure for oriental and possibly other sores.—E. W. Hayward, *Indian med. Gaz.*, May, 1933.

**Orisol** (*Pharmaceutical Specialities* (May & Baker) Ltd., London). Berberine acid sulphate in 2% solution for injection in the treatment of oriental sore.

**Dose.**—0.5 to 1.5 ml. is infiltrated round the edge of the sore and the procedure repeated at the end of a week.

**Berberina**,  $C_{20}H_{18}O_4N$ , crystallises in yellow needles with m.p. about 144°.

**Berberinæ Carbonas**,  $C_{20}H_{18}O_4N(HCO_3)_2 \cdot 2H_2O$ . Yellowish-brown crystals soluble in hot water and in alcohol; insoluble in cold water.

**Berberinæ Hydrochloridum** is the neutral salt,  $C_{20}H_{12}O_4 \cdot NCl \cdot 2H_2O$ , occurring in bright yellow crystals soluble in water about 1 in 400.

**Berberinæ Phosphas** is the acid phosphate,  $C_{20}H_{14}O_4N(H_2PO_4) \cdot H_3PO_4 \cdot 1\frac{1}{2}H_2O$ . Bright yellow crystals soluble 1 in 15 of water.

**Berberis** (*B.P.C.*). The dried stem of *B. aristata* (Berberidaceæ). A bitter tonic used in intermittent fevers. An extract from various species, combined with opium, is used in India as a local application in affections of the eye.

Liquor Conc., *I.c. Add.*, 1900. *Dose.*— $\frac{1}{2}$  to 1 drachm. Alcohol 20%, 1 in 2.

**Tinctura Berberidis** (*B.P.C.*). *Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.). 1 in 10.

Berberis berries (Baies) are official in *Fr. Cx.* as ingredient in Electuaire diascordium.

[P1-81] **Cotarninæ Chloridum** (*B.P.C.*). *Syn. and Prop. Names.* COTARNINE HYDROCHLORIDE (*P. Ned. V, F.E. VIII, P.G. VI, P. Helv. V*), OKISTYPTIN (*Richter, London*), STYPTARNIN (*Allen & Hanburys, London*), STYPTICIN (*Merck, Darmstadt; Martindale, London*).  $C_{12}H_{14}O_3NCl \cdot 2H_2O = 291.6$ . *P. Helv. V* has  $1\frac{1}{2}$  to 2  $H_2O$ .

[P1] "*Alkaloids, the following; their salts, simple or complex:—Cotarnine.*"

[81] "*Alkaloids, the following; their salts, simple or complex:—Cotarnine except substances containing less than 0.2% of cotarnine.*"

*Dose.*— $\frac{1}{2}$  to  $1\frac{1}{2}$  grains (0.02 to 0.1 g.) internally or hypodermically in special cases up to 4 grains in 10% solution.

The salt of the base cotarnine, in primrose coloured, deliquescent granular crystals, very soluble in water and alcohol.

*Uses.* The salts of cotarnine excite the isolated uterus on contact and they have been employed locally and systemically to check bleeding, especially in menstrual disorders, but the evidence as to their therapeutic value is contradictory. They do not affect the coagulation-time of the blood.

They have been employed internally in menorrhagia and in bleeding from uterine fibroids, or a 1 to 2% solution may be used locally on a tampon.

Erysipelas, eczema and shingles have been treated with a 5% ointment. A 2% ointment in a basis of wool-fat ointment is said to be useful in herpes and ulcerative balanitis. In more acute similar complaints up to 10% strength can be employed.

[P1-81] **Cotarnine Phthalate.** *Prop. Name.* STYPTOL (*Knoll, London*).  $(C_{12}H_{15}NO_4)_2C_8H_4COOH \cdot COOH = 640.3$ .

*Dose.*— $\frac{3}{4}$  grain (0.05 g.), but much larger doses are given by some practitioners, e.g., 10 grains, without unpleasant effects, every 2 to 3 hours.

A pale yellow crystalline powder, m.p.  $113^\circ$ , consisting of the acid phthalate. Soluble 1 in 60 of water. Contains 59% of cotarnine.

**Lodal** (*Burroughs Wellcome, London*). 6-7-Dimethoxy-2-methyl-3:4-dihydroisoquinolinium, an oxidation product of laudanone, in 1 gr. tablets. For the control of uterine hæmorrhage. *Dose.*—1 or 2 tablets thrice daily.

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[P1-81] **Cotarnina**,  $C_{17}H_{15}O_4N$ , is obtained by oxidising narcotine with nitric acid. In colourless needles, m.p.  $132^\circ$  to  $135^\circ$ , sparingly soluble in water, soluble in alcohol and ether.

Cotarnine is generally regarded as anomalous in containing water which cannot be removed, while the dried hydrochloride is anhydrous. But if the latter is regarded as cotarnine chloride and the base as cotarnine hydroxide, there is nothing anomalous.—D. B. Dott, *Chem. & Drugg.*, 1/1932, 14.

## HYDROGENII PEROXIDUM



**Liquor Hydrogenii Peroxidi** (*B.P., U.S.P. XI*). *Syn.* LIQUOR HYDROGENII DIOXIDI, HYDROGENIUM PEROXYDATUM DILUTUM (*P. Helv. V*), SOLUTÉ OFFICINAL D'EAU OXYGÉNÉE (*Fr. Cx.*).

*Dose.*— $\frac{1}{2}$  to 2 drachms (2 to 8 ml.).

May be prepared by the action of diluted sulphuric acid on barium peroxide in presence of water. A colourless liquid with harsh metallic taste.

1 ml. yields about 10 ml. of oxygen, equivalent to 2.5 to 3.5% *w/v* of  $H_2O_2$ . 20 and 100-volume strengths are also available.

**Incompatibility.** It readily decomposes, especially in contact with metallic oxides and readily oxidisable substances. Among the more important incompatibilities are alkalis, ammonia, arsenious salts, glycerin, hypophosphites, iodides, mercurous salts, phenol, potassium bromide, chlorinated soda and chlorine water.

Ether restrains decomposition and is used for making ozonic ether.

**Uses.** Internally is non-poisonous, and has been given for pertussis, flatulent dyspepsia and other affections, but now it is mostly employed locally as an antiseptic not precipitated by albumin. It is useful for assisting in removing surgical dressings which adhere obstinately. It is valuable used *undiluted* as a pigment, or diluted 1 in 8 as a spray, for diphtheria, tonsillitis, hay fever, laryngeal tuberculosis, putrid bronchitis and non-syphilitic ozæna; and as an antiseptic mouth-wash or gargle. For tuberculous and syphilitic ulcers, gangrene, malignant pustule and for purulent discharges it is antiseptic. It is astringent, *e.g.*, in epistaxis, and styptic in removing polypi. May be used locally for favus and other skin affections, also in gonorrhœa (up to 10-volume strength) occasionally. Wasp and hornet stings are at once relieved. It is sometimes used as an eye lotion, undiluted, in gonorrhœal conjunctivitis, or diluted 1 in 10 in diphtheritic conjunctivitis.

The 10-volume solution, preferably diluted with an equal volume of water, may be used in otorrhœa and otitis. After syringing out with weak boric acid lotion, allow to remain in 15 minutes, syringe out again, and dry carefully. Neutralising hydrogen peroxide solution with calcium carbonate and filtering is said to obviate the pain caused by syringing wounds in the ear with the

ordinary acid preparation. This, of course, must be done only at the time of use as the neutral solution rapidly loses its strength.

The 20-volume strength can be used for acute or chronic and gouty periodontitis by syringing out pockets around affected teeth, and also for septic root canals.

Solution of hydrogen peroxide is also used for bleaching hair and fabrics, but gangrene of the scalp has been known to follow the use of a 30% solution.

**ACHLORHYDRIA.** In about 75% of cases of achlorhydria the power of secreting acid can be restored by dieting, removal of septic foci and lavage of the stomach, when fasting in the morning, with dilute hydrogen peroxide ( $\frac{1}{2}$  oz. to the pint) to remove mucus. Treatment is continued daily until the washings are clear.—A. F. Hurst, *Pharm. J.*, ii/1934, 675.

**OTITIS MEDIA.** Peroxide drops dangerous, and increase percentage of mastoid infections.—Sir R. Woods. Its use should be abandoned in all cases.—J. B. Hogan. Opposed to its use.—H. Barwell—Discussion B.M.A. Ann. Meeting, 1933; *Brit. med. J.*, ii/1933, 255.

*Dangers of hydrogen peroxide in treatment of otorrhœa.* In contact with pus it yields a large quantity of oxygen which may cause serious symptoms and even death.—*Prescriber*, 1926, 69.

**Preservatives.** The following substances have been added to solution of hydrogen peroxide as preservatives:—benzoic acid 0.05%, phenacetin 0.1%, ethyl alcohol 10%, and acetanilide 0.002% with hydrochloric acid 0.02% (but *vide infra*).

The variation in the efficacy of hydrogen peroxide solutions is not due to a loss of strength, but to the stabiliser it contains. Sulphuric acid is shown to be unsuitable for the purpose as it inhibits the action of the catalase enzyme in blood, pus and saliva, which decomposes the hydrogen peroxide. From experiments described it would appear that suitable stabilisers are urea, phenazone and possibly hexamine, which do not inhibit the action of catalase.—S. M. Tritton, *Quart. J. Pharm.*, 1939, 446.

Nipagin is the best preservative for hydrogen peroxide; after storage in the absence of light and air for 2 years a 7.3% solution containing 0.1% of Nipagin still contained 7.1% of  $H_2O_2$ . Without preservative no  $H_2O_2$  was present. Acetanilide is oxidised by hydrogen peroxide to nitrobenzene and is a dangerous stabiliser.—K. Hill, *Apothekerztg. Berl.*, 1939, 54, 946.

**Solutio Hydrogenii Peroxydi Concentrata** (*P. Helv. V, P. Ned. V Supp. II*). *Syn. and Prop. Name.* SOLUTÉ CONCENTRÉ D'EAU OXYGÉNÉE (*Fr. Cx.*), PERHYDROL (*Merck, Darmstadt; Savory & Moore, London*).

A solution of hydrogen peroxide containing about 30% *w/v* of  $H_2O_2$  and yielding a hundred volumes of oxygen. It is more stable than weaker solutions and can be conveniently used for their preparation.

**Collutorium Hydrogenii Peroxidi.** Hydrogen peroxide solution (20 volume) 500, oil of peppermint 1, elixir of saccharin 30, thymol water 470.

**Astringent Hydrogen Peroxide Mouth-Wash.** The above with 5% of solution of aluminium acetate added. *Dilute either of the above with 7 parts of water.* For painful ulcers of the mouth in syphilis.

**Gargarisma Hydrogenii Peroxidi.** Hydrogen peroxide solution 1 dr., sodium chloride 5 gr., glycerin 30 m., water to 1 oz.

**Guttæ Hydrogenii Peroxidi et Spiritus** (*St. T. H.*).

Hydrogen peroxide solution and industrial methylated spirit, equal parts. Used as ear drops.

Best dispensed in separate bottles because on standing acetaldehyde and acetic acid are formed, and may cause irritation or a stinging sensation when used.—W. A. Woodard and J. Pickles, *Quart. J. Pharm.*, 1934, 418.

**Unguentum Hydrogenii Peroxidi.**

Hydrogen peroxide solution 10, anhydrous wool fat to 100. To be freshly made. Useful in eczema and other parasitic skin affections.

**Bidrox** (Evans, Sons, & Lescher & Webb, Liverpool). A stable brand of hydrogen peroxide.

**Dioxogen** (Allen & Hanburys, London). A 12-volume solution of hydrogen peroxide.

**Ozonic Ether.**

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Prepared by shaking a strong solution of hydrogen peroxide with ether and separating the ethereal layer. It yields 4 to 5 volumes of oxygen.

It is miscible with alcohol and with water in all proportions up to 3 times its volume. Is more stable than solution of hydrogen peroxide. In conjunction with tincture of guaiacum, it is employed as a test for blood, v. Vol. II. Has been given internally for whooping cough.

**Solid Hydrogen Peroxide.** *Prop. Name.* HYPEROL (Richter, London).

A solid compound of hydrogen peroxide and urea, stabilised with a trace of citric acid. The compound contains about 35% of hydrogen peroxide and is stable below 60°. A 10% solution is approximately the same strength as solution of hydrogen peroxide (10 volume).

**Calcii Peroxidum** (B.P.C.). *Syn.* CALCII SUPEROXYDUM, GORIT.  
 $\text{CaO}_2 = 72.08$ . Crystals containing  $8\text{H}_2\text{O}$  are obtainable.

*Dose.*—3 to 8 grains (0.2 to 0.5 g.) daily.

A white crystalline powder slightly soluble in water, evolving oxygen. It explodes if mixed with glycerin or formalin.

A useful intestinal antiseptic, given in milk, for infants, e.g., in summer diarrhoea. Recommended in hyperacidity; also in soil-contaminated wounds and in dentifrices.

**Magnesii Peroxidum** (B.P.C., *Fr. Cx.*).  $\text{MgO}_2 = 56.32$ .

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 g.).

A white tasteless powder insoluble in water, containing not less than 15% of  $\text{MgO}_2$  with magnesium oxide. *Fr. Cx.* requires not less than 25%.

Used where increased oxidation is desired; given in diarrhoea of phthisis, vomiting, anorexia, flatulence and pyrosis. 10 gr. every four hours are administered in typhoid fever. 5 to 10% added to precipitated or prepared chalk powder makes a good dentifrice.

**Dentifricium Oxidans** (R.D.H.). Powdered hard soap 30 gr., powdered orris 30 gr., magnesium peroxide 1 dr., menthol 1 gr., oil of clove 2 m., precipitated chalk to 1 oz.

[P1] **Magnocarbon** (Richter, London). Charcoal 4 gr., magnesium peroxide 4 gr., extract of belladonna  $\frac{1}{2}$  gr. *Dose.*—1 or 2 tablets thrice daily. In hyperacidity, dyspepsia, flatulence and ulcer.

**Magnozon** (Richter, London). Magnesium peroxide. *Dose.*—5 to 30 grains in tablet form.

**Magnesium-Perhydrol** (Merck, Darmstadt; Savory & Moore, London) contains 25% of  $\text{MgO}_2$ .

**Sodii Peroxidum.** *Syn.* SODIUM DIOXIDE, F.E. VIII; OXYLITH, "SOLID OXYGEN."  $\text{Na}_2\text{O}_2 = 77.99$ .

A yellowish white amorphous hygroscopic powder, dissolves in water with production of heat and evolution of oxygen. 50% solution has been used in dentistry to whiten stained teeth. Technically used as bleach for sponges, wool, bones, oils, etc.

**Unguentum Sodii Peroxidi.** 20% in soft white paraffin may be tried with caution in acne.

**Zinci Peroxidum** (*Fr. Cx.*, *P. Dan.*). *Syn.* DERMAGEN.

A mixture of zinc oxide and zinc peroxide ( $\text{ZnO}_2 = 97.38$ ) containing about 35% of the latter. It is a white powder *insoluble* in water.



Used locally in skin affections. Promotes healing of chronic ulcers. For burns and wounds.

**DIABETIC GANGRENE.** Zinc peroxide markedly inhibits the growth of the hæmolytic streptococci and all anaerobic bacteria, including the organisms causing gas gangrene and the anaerobic streptococci. It neutralises or inactivates the toxins formed by these organisms and stimulates the formation of granulation tissue. The zinc peroxide should be suspended in sterile distilled water and applied to every part of the wound surface, which is then covered with fine meshed gauze soaked in the same suspension. This is covered with compresses saturated with sterile distilled water, and these in turn covered with impermeable material. The dressing should be changed every 24 hours, the old material irrigated off, and a new dressing applied.—F. L. Meleney, per *J. Amer. med. Ass.*, i/1940, 623.

**MALIGNANT LESIONS.** The use of zinc peroxide paste in radio-necrotic ulcers, with and without tumour growth, is effective in controlling fetor, infection and pain. The wound is cleaned with peroxide and saline sprays, free necrotic tissue removed and the wound again sprayed. A preparation of sterilised zinc peroxide is mixed with an equivalent amount of sterile distilled water, and more water added until the paste has a consistency of about 40% cream; this is applied by syringe to the entire lesion. Gauze is soaked in the suspension and applied throughout the lesion. The whole is covered with sterile pads soaked in distilled water, and the wound packed against evaporation by several layers of petrolatum or zinc oxide gauze, the dressing being secured by a larger pad and bandage. The wound never requires dressing more than twice a day. In the treatment of oral lesions the zinc peroxide is applied as a thick paste every 3 hours, and a 1 to 3 suspension is used as a mouth-wash. Throat lesions receive a spray of a 1 to 2 suspension and a paste applied directly to the lesion.—B. S. Freeman, *J. Amer. med. Ass.*, ii/1940, 181.

**ULCERS.** Zinc peroxide in powder suspended in an equal quantity of sterile distilled water, making a mixture of cream consisting of about 40% is a valuable treatment for open wounds and chronic ulcers.—F. L. Meleney, *N. Y. St. J. Med.*, 1939, 39 2188.

Ulcers due to microaerophilic streptococci have been successfully treated with a paste made of zinc peroxide and water.—B. Fantus and H. A. Dyniewicz, *J. Amer. pharm. Ass.*, 1939, 548.

## HYOSCYAMUS

*B.P.*, *U.S.P. XI*, *Fr. Cx.*, *P. Jap. V*, *P. Helv. V*, *P. Dan.*

*Syn.* HYOSCYAMI FOLIA, HYOSCYAMUS LEAVES, JUSQUIAME (*Fr. Cx.*), HENBANE LEAVES.

[P1] "*Alkaloids, the following; their salts, simple or complex:—Atropine; Hyoscine; Hyoscyamine.*"

[S1] "*Alkaloids, the following; their salts, simple or complex:—Atropine except substances containing less than 0.15% of atropine; hyoscine except substances containing less than 0.15% of hyoscine; hyoscyamine except substances containing less than 0.15% of hyoscyamine.*"

*Dose.*—3 to 6 grains (0.2 to 0.4 g.). *U.S.P. XI* average dose 3 grains. *P. Helv. V* has max. single dose 15 grains, max. in 24 hours 45 grains.

Hyoscyamus consists of the dried leaves and flowering tops of *Hyoscyamus niger* (Solanaceæ); it contains not less than 0.05% of alkaloids calculated as hyoscyamine. *Fr. Cx.* specifies the

leaves collected during the flowering stage and containing 0.2% of alkaloids, and the seeds.

**Uses.** Similar to those of belladonna and stramonium.

Colocynthis and other strong purgatives in pills are rendered less painful in action by addition of extract of hyoscyamus.

**Antidotes.** Treat as for poisoning by atropine, *see* p. 237.

[P1] **Extractum Hyoscyami Liquidum (B.P.).**

**Dose.**—3 to 6 minims (0.2 to 0.4 ml.).

Contains 0.05% of alkaloids calculated as hyoscyamine. 6 minims contain about  $\frac{3}{16}$  gr. of alkaloids.

[P1-S1] **Extractum Hyoscyami Siccum (B.P.).** *Syn.* EXTRACTUM HYOSCYAMI.

**Dose.**— $\frac{1}{4}$  to 1 grain (0.016 to 0.06 g.). The dose in the B.P. '14 was 2 to 8 gr.; the reduction was made to bring the dose of extract into line with that of other hyoscyamus preparations.

It is prepared by the same method as Ext. Belladonnæ Siccum. It conforms with I.A., and is standardised to 0.3% of alkaloids. *P. Helv. V, P. Ital. V and F.E. VIII,* 0.5% of alkaloids, and *P. Ned. V Suppl. II* 0.125 to 0.150%; *P.G. VI* contains 0.5% of hyoscyamine. *Fr. Cx.* has 1.5% of total alkaloids in a firm extract containing 10% of water.

Extractum Hyoscyami (*P. Ned. V*) is required by the 2nd supplement to contain 0.125 to 0.150% of alkaloids. Extracts obtained by the author contained from 0.20 to 0.65%, and hence often required the addition of sugar equivalent to 4 times the weight of the extract to reduce the alkaloid content to the required figure, the preparation thus obtained being more correctly described as "Syrupus."—J. A. C. Van Pinxteren, *Pharm. Weekblad.*, 1939, 76, 1629.

[P1-S1] **Extractum Hyoscyami (U.S.P. XI).** *Average dose.*— $\frac{1}{8}$  grain (0.05 g.).

In two forms, pillular and powdered; they contain 0.15% of alkaloids and are therefore about half the strength of the B.P. 1932 dry extract.

[P1-S1] **Succus Hyoscyami (B.P.C.),** *dose*— $\frac{1}{4}$  to 1 drachm (2 to 4 ml.), is the juice expressed from fresh hyoscyamus and preserved with alcohol.

[P1] **Tinctura Hyoscyami (B.P.).**

**Dose.**— $\frac{1}{4}$  to 1 drachm (2 to 4 ml.). 1 drachm contains about  $\frac{3}{16}$  gr. of alkaloids.

Prepared with 10% v/v of liquid extract of hyoscyamus in alcohol 70%, and contains 0.005% w/v of alkaloids. *Fr. Cx.* prepares by percolation of the leaves (1 in 10) with alcohol 70%.

Some samples give a precipitate of green colouring matter on dilution with water.

[P1] **Tinctura Hyoscyami (U.S.P. XI).** *Average dose.*—30 minims (2 ml.).

Contains 0.004% of alkaloids and is therefore about four-fifths the strength of the B.P. tincture.

[P1] **Huile de Jusquiame Composée (Fr. Cx.).** *Syn.* BAUME TRANQUILLE.

Macerate powdered leaves of belladonna, hyoscyamus, *Solanum nigrum*, poppy and stramonium, of each 50, with alcohol 200, and allow to stand 24 hours; then add poppy seed oil 5000, warm for 6 hours at 60° to 70°, press and allow to deposit, and finally add oils of lavender, peppermint, rosemary and thyme, of each 1, and filter.

[P1] **Hyoscyami Semen (B.P.C.).** *Syn.* HENBANE SEED.

The seeds of *H. niger*, containing about 0.05 to 0.1% of alkaloid, chiefly hyoscyamine, and 20% of oil.

[P1] **Meglin's Pills.** Hyoscyamus extract, valerian extract, and zinc oxide each 1 grain. In sciatica.

**Mictasol** (*Bengué, London*). Tablets of malva purpurea, hexamine and camphor bromide. *Dose.*—2 to 3 thrice daily. [P1] Suppositories are similar, but contain also extract of hyoscyamus. For nephritis, cystitis, hæmorrhoids, etc.

[P1-S1] **Herba Hyoscyami mutici** (*P. Helv. V*). *Syn.* JUSQUIAME D'ÉGYPTE, EGYPTIAN HENBANE. From *H. muticus*, and contains not less than 0.8% of alkaloids, chiefly hyoscyamine. *P. Helv. V* permits it to be used for making standardised galenicals, but it must not be dispensed for hyoscyamus.

[P1-S1] **Hyoscyamina** (*Fr. Cx.*).  $C_{17}H_{23}O_3N = 289.2$ .

*Dose.*— $\frac{1}{100}$  to  $\frac{1}{1000}$  grain (0.0003 to 0.0006 g.), in cases of mania increased to  $\frac{1}{10}$  or  $\frac{1}{5}$  grain, dissolved in water by means of diluted sulphuric acid, or in a pill.

An alkaloid obtained from various Solanaceous plants, *Hyoscyamus muticus* being the best source. It is the *levo* isomer of atropine (which is *dl*-hyoscyamine) into which it can be converted by heating or by the action of alkali. It is in light, snow-white crystals, m.p. 108° to 109°.

**Soluble** 1 in 120 of water, freely in alcohol, 1 in 1 of chloroform, 1 in 48 of ether, 1 in 110 of benzene and slightly in light petroleum.

**Antidotes.** Treat as for poisoning by atropine, see p. 237.

[P1-S1] **Hyoscyaminæ Hydrobromidum.**  $C_{17}H_{23}O_3N.HBr = 370.1$ .

*Dose.*— $\frac{1}{100}$  to  $\frac{1}{1000}$  grain (0.0003 to 0.0006 g.), increased.

In small white crystals, m.p. 152°, soluble about 2 in 1 of water, also soluble in alcohol 90%.

[P1-S1] **Hyoscyaminæ Sulphas** (*B.P.C.*).

$(C_{17}H_{23}O_3N)_2.H_2SO_4 = 676.5$ .

*Dose.*— $\frac{1}{100}$  to  $\frac{1}{1000}$  grain (0.0003 to 0.0006 g.), increased up to  $\frac{1}{10}$  grain (0.006 g.) in mania.

In small white granular deliquescent crystals, soluble 2 in 1 of water and about 1 in  $4\frac{1}{2}$  of alcohol 90%.

**Uses.** As a mydriatic it acts like atropine, but with greater intensity, while the duration of effect is about equal.

It removes the pain of neuralgia, and is given for mental excitement, e.g., delirium tremens. In mania  $\frac{1}{5}$  grain may be given hypodermically. It is used to relieve the tremor, rigidity, and excessive salivation in paralysis agitans. Is useful for prevention of sea-sickness; tablets or granules of  $\frac{1}{100}$  gr. may be taken occasionally a day or two beforehand, and for the first few days on board; hourly if required.

[P1-S1] **Hyoscina.** *Syn.* SCOPOLAMINE.  $C_{17}H_{21}O_4N = 303.2$ .

A thick syrupy alkaloid, contained in *Hyoscyamus niger*, different species of *Scopola*, *Datura alba*, the flowers of which yield 0.5%, and other solanaceous plants. It may be obtained from the mother liquors of the preparation of hyoscyamine.

**Antidotes.** Treat as for poisoning by atropine, see p. 237.

**Uses.** Hyoscine base is used as a mydriatic in oily solution or as an ointment. Mydriasis is quick in onset and of short duration. For the preparation of aqueous solutions and for oral and hypodermic use a water-soluble salt is used, usually the hydrobromide.

[P1-81] **Oleum Hyoscinae (R.L.O.H.)**. Hyoscine 4 gr. dissolved in minimum amount of chloroform and mixed with castor oil at 61° to 1 oz. Causes a mydriasis which is certain, quick in onset and of short duration.

[P1-81] **Oleum Hyoscinae (P.Helv. V)** is 1% in arachis oil,

[P1-81] **Unguentum Hyoscinae (R.L.O.H.)**. Syn. UNGUENTUM SCOPOLAMINÆ. Hyoscine 1 or 2 gr. dissolved in minimum amount of chloroform and mixed with yellow soft paraffin at 61° to 1 oz.

[P1-81] **Hyoscinae Hydrobromidum (B.P.)**. Syn. SCOPOLAMINÆ HYDROBROMIDUM (U.S.P. XI, Fr. Cx., P. Ned. V, P. Jap., P. Belg. IV, F.E. VIII, P. Dan., P. Ital. V).

$C_{17}H_{21}O_4N \cdot HBr \cdot 3H_2O = 438.1$ . P. Helv. V has  $2H_2O$ .

**Dose.**— $\frac{1}{100}$  to  $\frac{1}{10}$  grain (0.0003 to 0.0006 g.). The dose may be increased to  $\frac{1}{50}$  grain. Fr. Cx. and P.G. VI have max. single dose 0.001 g., max. daily dose 0.003 g. U.S.P. average dose  $\frac{1}{100}$  grain.

The hydrobromide of *l*-hyoscine. In white rhombic crystals, soluble 1 in 2 of water, 1 in 13 of alcohol 90%. Melts at 194° to 196° after drying at 100° (U.S.P. XI 190° to 192°).

**Uses.** Produces prompt depression of the motor area of the brain, and acts as a powerful hypnotic; especially useful in acute mania and delirium, including delirium tremens, calming the excitement and rapidly inducing sleep. For this purpose a dose of  $\frac{1}{50}$  gr. with morphine  $\frac{1}{4}$  gr. is said to give excellent results. Occasionally a short stage of excitement precedes sleep and, in general, it is a less reliable hypnotic than chloral hydrate or morphine. It is also useful in chorea, asthma and pertussis, and is employed in the intensive withdrawal treatment of morphine addiction (see under Morphina). Hyoscine hydrobromide is extensively used in the symptomatic treatment of paralysis agitans and post-encephalitic parkinsonism; doses of  $\frac{1}{100}$  to  $\frac{1}{50}$  gr. thrice daily *per os* often greatly relieve the tremors and muscular rigidity. If pilocarpine is given simultaneously to prevent dryness of the mouth and paralysis of accommodation the dose can frequently be increased to  $\frac{1}{50}$  gr. and occasionally to  $\frac{1}{4}$  gr. thrice daily. In conjunction with morphine, hyoscine is used for the induction of "twilight sleep" in labour (*vide infra*). Hyoscine hydrobromide is also used as a mydriatic in 1% aqueous solution or as the eye ointment or lamella.

**BASAL NARCOSIS.** The following combination of drugs offers practically all the advantages of Avertin as a pre-anæsthetic without certain of its disadvantages in the hands of inexperienced anaesthetists. About an hour before the operation the patient receives a subcutaneous injection of morphine hydrobromide  $\frac{1}{4}$  gr., hyoscine hydrobromide  $\frac{1}{100}$  gr., and atropine hydrobromide  $\frac{1}{200}$  gr. (Tab. Hyoscinae Co., P.D. & Co.) and an intragluteal injection of Somnifaine 2 ml. The combined action of these drugs leaves the pupil practically normal, so that the size of the pupil still provides a useful guide to the depth of chloroform or ether anaesthesia. The amount of ether required is about half that which would be required without the addition of Somnifaine, the post-anæsthetic vomiting is greatly reduced, and amnesia is complete in about 90% of cases and usually continues for about 24 hours. There is a long post-anæsthetic sleep lasting about 6 hours. With this combination there is a noticeable freedom from shock.—W. N. Leak, *Brit. med. J.*, ii/1939, 1162.

**ENCEPHALITIS, EPIDEMIC.** Hyoscine of undoubted value, though effect is temporary. Start with  $\frac{1}{10}$  grain once a day hypodermically, increased if necessary to  $\frac{1}{5}$  grain. *Per os* larger doses may be employed thrice daily, preferably after meals.—P. K. McCowan and co-workers, *Brit. med. J.*, i/1926, 779; *Lancet*, i/1926, 802.

**INFANTILE CEREBRAL PALSY.** This condition, which is characterised by one or more of the following features: spasticity, tremor, inco-ordination, choreiform and athetoid movements and mental deficiency, responds well to hyoscine treatment. The usual maintenance dose is  $\frac{3}{16}$  gr. of hyoscine hydrobromide twice daily by mouth. Drooling was stopped, athetosis lessened, confidence increased, relaxation improved and progress in retraining more rapid. One child learned to walk in three days. The favourable response came early or not at all.—I. C. Nicholls and S. R. Watson, *New Engl. J. Med.*, ii/1939, 888.

**PARALYSIS AGITANS.** The medicament of choice.—W. Freeman, *J. Amer. med. Ass.*, ii/1927, 1320.

Paralysis agitans treated. Give a mixture of hyoscine  $\frac{3}{16}$  gr. with pilocarpine nitrate  $\frac{1}{4}$  gr. and solution of strychnine hydrochloride 3 m. 4 times daily, gradually increased until the tremor is controlled.—A. F. Hurst, *Brit. med. J.*, i/1926, 845.

**POST-ENCEPHALITIC PARKINSONISM.** Hyoscine hydrobromide produces quite definite and even marked improvement.—A. J. Hall, *Brit. med. J.*, i/1926, 129.

Chronic encephalitis treated with hyoscine hydrobromide  $\frac{1}{16}$  gr. thrice daily, and with harmine.—*Lancet*, ii/1929, 794.

Marked relief in chronic cases of parkinsonism and disturbance of sleep, following continued administration of hyoscine hydrobromide  $\frac{1}{16}$  gr. thrice daily by mouth, but not curative and symptoms returned on suspension.—A. G. Robb, *Brit. med. J.*, ii/1925, 646.

[P1-S1] **Guttæ Hyoscinæ (R.L.O.H.).** 1 or 2 grains to 1 ounce.

[P1] **Hausus Hyoscinæ (Mid. H.).**

Hyoscine hydrobromide  $\frac{1}{16}$  gr., compound tincture of lavender 5 m., chloroform water to 1 oz. For the sequelæ of encephalitis lethargica.

[P1-S1] **Lamellæ Hyoscinæ.** *Syn.* LAMELLÆ SCOPOLAMINÆ (R.L.O.H.) contain  $\frac{3}{16}$  gr.,  $\frac{1}{16}$  gr. or  $\frac{3}{16}$  gr. grain.

[D-P1-S1] **Nebula Hyoscinæ Composita (B.P.C.).** An aqueous spray containing hyoscine hydrobromide 0.057% w/v, cocaine hydrochloride about 0.9% w/v, and atropine sulphate about 0.1% w/v.

[P1] **Oculentum Hyoscinæ (B.P.).** 0.125% of hyoscine hydrobromide in simple eye ointment.

### Scopolamine-Morphine Anæsthesia.

Hyoscine hydrobromide,  $\frac{1}{16}$  to  $\frac{1}{8}$  gr. or more, and a salt of morphine  $\frac{1}{4}$  to  $\frac{1}{2}$  gr., are injected on the evening before the operation, and a similar or higher dose in the morning before the operation. This alone may suffice to produce deep sleep. If not, ether or chloroform may be given until complete anæsthesia occurs. Patients sleep for hours through the first painful periods after the operation.

Morphine-scopolamine narcosis advocated for routine use as a preparation for surgical anæsthesia in children over one year of age. The solution, given hypodermically, contains 0.01 g. of morphine and 0.0005 mg. of scopolamine per ml. At 12 years the whole dose is injected; under 10, three-quarters; under 6, a half; under 4, a third; under 2, a quarter. Anæsthesia begun and consciousness regained with much less distress, and danger of syncope at onset reduced. Employed without ill-effect in over 800 children.—P. F. Armand-Delille, *Bull. Acad. Méd., Paris*, 1932, 890.

The "Twilight Sleep" method of inducing child-birth was introduced with the object of enabling the woman to pass through labour without either the consciousness or remembrance of pain. One of the physiological effects of scopolamine is to induce temporary loss of memory, and it is employed for this purpose in conjunction with morphine, both drugs being given by hypodermic injection. The first injection is given as soon as labour has begun and consists of  $\frac{1}{8}$  to  $\frac{1}{4}$  gr. of morphine and  $\frac{1}{16}$  to  $\frac{1}{12}$  gr. of

scopolamine, the larger dose in each case being reserved for the strong, robust type of primipara. The patient is put to bed and the room darkened and all noise excluded. *The morphine must not be repeated*, but the scopolamine may be repeated as often as is necessary to produce amnesia, the second injection of  $\frac{1}{10}$  gr. being given at the end of the first hour and subsequently at hourly intervals.

While the method has certain advantages, it is not as successful as was originally claimed, and it is subject to some serious disadvantages, of which the most important are the frequency of cyanosis, both of mother and child, the constant supervision required, and the complete failure to produce narcosis in a certain number of cases. See also Gwathmey's Synergistic Theory (Magnesium Sulphate and Morphine), p. 150.

Scopolamine-morphine narcosis in labour. In 25% of cases result very good, in 15% good, and in 10% no benefit.—J. S. Quin, *Lancet*, i/1929, 668. "Twilight Sleep" given as routine in hundreds of cases.—G. W. Theobald, *Brit. med. J.*, ii/1930, 664.

Three doses of hyoscine hydrobromide given hypodermically at  $\frac{1}{2}$ -hourly intervals when regular pains commence (in primiparae when cervix is three fingers dilated), and repeat every 2 hours as long as labour lasts. Up to  $\frac{1}{10}$  gr. used without ill effect. Chloroform given in second stage. Important not to omit last (third) injection, even if child about to be born. Excellent results and no ill effects on babies.—A. M. Claye, *Brit. med. J.*, ii/1931, 12.

Hyoscine  $\frac{1}{10}$  gr. in 2 ml. of 50% magnesium sulphate solution adopted as routine as a reasonable analgesic in labour. Safe and fairly effective. One dose usually enough.—R. Kelson Ford, *Brit. med. J.*, ii/1930, 726.

An analysis of 50 cases of amnesia in labour using hyoscine hydrobromide alone. Entirely safe for mother and child. Labour not delayed, puerperal morbidity not increased, and babies born without circulatory or respiratory defects: not suitable for domiciliary midwifery.—T. Barnett, *Brit. med. J.*, i/1934, 940.

[P1-81] **Genoscopolamine** (*Amido Laboratories, Paris; Wilcox, Jozseau, London*). Nitrogen oxide of scopolamine in granules containing 0.5 mg. (dose—2 three times daily), drops (dose—20 drops = 1 mg. of Genoscopolamine, three times daily), or ampoules of 1 ml. (= 1 mg.) for subcutaneous injection. Has a therapeutic action similar to that of scopolamine but is less toxic.

[P1-81] **Vasano** (*Schering, London*). Camphoric acid salts of l-scopolamine and l-hyoscyamine. Dose.—2 dragées each of 0.0075 gr. Prophylactic against travel sickness.

[P1-81] **Duboisine Sulphate**. Dose.— $\frac{1}{10}$  to  $\frac{1}{5}$  grain (0.00025 to 0.001 g.). An alkaloidal sulphate from *Duboisia myoporoides* (Solanaceae) consisting chiefly of hyoscyamine sulphate. A deliquescent yellowish-white crystalline powder. Used as a mydriatic in solution (0.2 to 0.5%) or ointment.

Samples of Australian *Duboisia myoporoides* contain hyoscine but no trace of hyoscyamine. In addition they contain four new alkaloids: tiglyl-pseudo-tropeine, mono-isovaleryl-dihydroxytropeine, isovaleryl-nortropeine, and d- $\alpha$ -methylbutyrylnortropeine. A commercial sample of duboisine sulphate was found to consist almost entirely of hyoscyamine sulphate with no trace of hyoscine.—G. Barger, W. F. Martin and W. M. Mitchell, *J. chem. Soc.*, 1937, 1820; *ibid.*, 1938, 1685.

[P1-81] **Guttæ Duboisinæ** (R.L.O.H.). Duboisine sulphate 1 gr., sterilised water to 1 oz.

[P1-81] **Dulcamara** (B.P.C.). *Syn.* WOODY NIGHTSHADE, BITTER-SWEET (*Fr. Cx.*).

The dried stem and branches of *Solanum Dulcamara* (Solanaceæ). Alterative and diuretic; was formerly used in dropsy and in psoriasis and other skin diseases. Now practically obsolete.

[P1] **Infusum Dulcamaræ.** 1 in 10. *Dose.*—1 to 2 ounces.

[P1] **Lactuca (B.P.C.).** *Syn.* LETTUCE, WILD LETTUCE.

The fresh flowering herb, *L. virosa* (Compositæ). A mild sedative and hypnotic; used in irritable cough. Contains traces of a mydriatic alkaloid, possibly hyoscyamine.

[P1] **Extractum Lactucæ (B.P.C.).** *Dose.*—5 to 15 grains (0.3 to 1 g.).

A soft extract prepared from the fresh juice. A mild sedative for cough.

**Lactucarium.** *Syn.* LETTUCE OPIUM. *Dose.*—5 to 15 grains (0.3 to 1 g.).

The dried latex of lettuce. Brownish masses with opium-like odour and bitter taste, partly soluble in alcohol and in ether.

[P1-S1] **Scopolia (B.P.C.).** *Syn.* SCOPOLA.

*Dose.*—1 to 2 grains (0.06 to 0.12 g.). The dried rhizome of *S. carniolica* (Solanaceæ).

Contains about 0.4% of alkaloids, chiefly hyoscyamine. Resembles belladonna in action but is seldom used.

[P1-S1] **Folium Scopolia (P. Jap. V).** The dried leaves of *S. japonica*, known as Japanese belladonna, and containing not less than 0.15% of hyoscyamine.

## ICHTHAMMOL

### B.P.

*Syn. and Prop. Names.* AMMONIUM ICHTHOSULPHONATE (*Fr. Cx.*), AMMONIUM SULPHO-ICHTHYOLATE (*P. Ital. V, F.E. VIII, P. Jap. V*), AMMONIUM SULFOBITUMINOSUM (*P. Helv. V*), AMMONIUM BITHIOLICUM (*P. Belg. IV*), ICHTHOSULPHOL, ICHTHYOL, PERICHTHOL (*British Drug Houses, London*), SUBITOL (*C. Zimmermann, London*).

*Dose.*—5 to 10 grains (0.3 to 0.6 g.).

A viscous, almost black substance with a disagreeable odour, consisting chiefly of the ammonium salts of the sulphonic acids of an oil prepared from a bituminous schist.

It contains not less than 10.5% of organically combined sulphur, and sulphur as sulphates is not more than one-quarter of the total S. It contains not more than 50% of water.

**Soluble** in water; partly soluble in alcohol 90% and in ether; miscible with glycerin and fixed oils.

**Uses.** Internally it is mildly antiseptic and irritant to the gastro-intestinal tract and has been given for rheumatism and skin affections, and as an intestinal antiseptic in constipation and dyspepsia. Externally it is used in chronic skin diseases, such as eczema, furunculosis, psoriasis and acne. Applied on wool as vaginal tampon, and used as pessaries and suppositories in cervicitis and vaginal discharges. For pruritus and ulcers a 10% solution is used, and may be combined with lead and mercury without the formation of sulphides. For burns it may be used mixed with zinc oxide or bismuth (the powder being spread

evenly over the surface), or in ointment (10 to 50%). In mumps the swelling and pain are said to be rapidly relieved by inunctions of equal parts of ichthammol and lanolin. Gonorrhœa has been treated by intramuscular injection of 2% solution (diluted just before use) in doses of 3 ml. every second or third day.

**ROSACEA.** In the first and second stages ichthammol is a most useful therapeutic agent; it should be applied locally in the form of lotions or ointments and internally in the form of pills or capsules commencing with 5 gr. on an empty stomach, morning and evening, increased to 7½ and then 10 gr. and upwards until the desired results are obtained.—A. Furniss, *Prescriber*, 1939, 382.

**Collodium Ichthammolis (B.P.C.).** Ichthammol 1 in simple collodium *q.s.* to 8. Used for eczema, erysipelas and other skin diseases.

**Collodium Ichthammolis cum Æthere (B.P.C.).** Ichthammol 1 in ether and simple collodium *q.s.* to 4.

**Gelatinum Zinci et Ichthammolis (B.P.C.).** *Syn.* PASTA ZINCI ET ICHTHAMMOLIS, UNNA'S PASTE WITH ICHTHAMMOL.

Ichthammol about 2% in a basis of zinc oxide and glycerogelatin.

**Glycerinum Ichthammolis (B.P.C.).** Ichthammol 10% *w/w* in glycerin.

**LYMPHANGITIS** well treated with glycerin and ichthammol.—H. W. Webber *Brit. med. J.*, i/1931, 206.

**Parogenum Ichthammolis (B.P.C.).** *Syn.* ICHTHAMMOL VASOLIMENT. 10% *w/v*.

**Oculentum Ichthammolis cum Zinci Oxido (Mid. H.).** Ichthammol 1, zinc oxide 15, yellow soft paraffin to 100. For chronic blepharitis.

**Pasta Ichthammolis (B.P.C.).** *Syn.* GELATINUM ICHTHAMMOL. Ichthammol 10% in a glycerogelatin basis.

**Pessus Ichthammolis** contains 10 gr. (0.6 g.) in glycerin suppository basis to 120 gr. For leucorrhœa.

Ichthammol pessaries are sometimes required to be made with oil of theobroma basis. They are also made with resorcinol 3%, and these must be made with oil of theobroma.

**Pilula Ichthammolis.**

Ichthammol 2½ gr., compound tragacanth powder ½ gr., powdered liquorice 1½ gr. Make a pill on hot plate if necessary.

**Suppositorium Ichthammolis (B.P.C.)** contains 3 grains of ichthammol in glycerin suppository basis.

Suppositories may contain 3 grains (0.2 g.) with a basis of theobroma 12 grains. The mixture must be almost "set" whilst pouring into the moulds, otherwise it may separate. The addition of beeswax is not desirable; indeed a large proportion will render the suppository quite insoluble. Ichthammol pessaries or suppositories in a glycerogelatin base must not be overheated or they may become insoluble.

If a stiffer preparation is required than that obtained with glycerin suppository mass, the following proportions are satisfactory:—Ichthammol 10, glycerin 60, gelatin 16, water 14.

Tampons may be prepared with 5, 10 or 20% of ichthammol in glycerin.

**Unguentum Ichthammolis (B.P.C.).** 10% in wool-fat ointment.

**Unguentum Ichthammolis Compositum (B.P.C.).** Ichthammol 9%, with sulphur, starch, resorcinol, betanaphthol and salicylic acid in wool-fat ointment.



**Unguentum Ichthammol et Zinci Oxidi** (R.L.O.H.) has ichthammol 8 gr., zinc oxide 15 gr., yellow soft paraffin to 1 oz.

**Ichtholdine** (Sharp & Dohme, London). A preparation containing ichthylol, iodine, phenol, hydrastine hydrochloride, boroglyceride and eucalyptol. For treatment of chronic inflammatory conditions of the mucous membranes, e.g., endometritis, ulceration of the cervix and vagina, etc.

**Thigenol** (Roche Products, Welwyn Garden City) is the sodium salt of a synthetic sulpho-oleic acid, containing 2.85% of S. Soluble in water, glycerin, alcohol; miscible with fats and oils. A 5% ointment relieves eczema. Tampons and pessaries also available.

[P2] **Vaginoids** (Sharp & Dohme, London). Suppositories containing ichthylol 1½ gr., phenol 2 gr., iodine (combined) ¼ gr., zinc phenolsulphonate 1 gr., in a glyco-gelatin basis. For ulcerations of the cervix and vaginal inflammations.

**Sphagnol** (Peat Products, London). A native tar product produced from peaty deposits. In blepharitis, eczema, piles, sores and burns. Detergent and relieves insect bites in tropical countries. Ointment (10%), Medical Soap (15%), Toilet Soap (5%), Shaving Soap (5%) and Suppositories (3 gr., for piles) are made.

## INFUSA

Infusions are dilute solutions of the water-soluble extractives of vegetable drugs, prepared by macerating the drugs in hot or cold distilled water for a short period of time, usually 15 minutes, and then straining. Cold water must be used if the drugs contain an appreciable amount of starch. Infusions are chiefly used as vehicles for other drugs, and are consequently of either an aromatic or bitter nature.

The infusions in the B.P. and B.P.C. are of two types:—(a) freshly prepared infusions which must be used within 12 hours of preparation, and (b) infusions prepared by diluting concentrated preparations with 7 times their volume of distilled water.

**Tisanes.** Infusions or teas (usual strength 1 in 10) of herbs are largely used by the laity in France, Italy, etc.

**Preservation.** Freshly-made infusions are preferable to preserved or concentrated infusions, but if it is necessary to store infusions the following methods are recommended in descending order of preference:—(1) Fresh infusions sterilised by heat and drawn off aseptically. (2) Concentrated infusions made with water and treated similarly. (3) Concentrated infusions preserved with alcohol, 10% being required for infusions of clove and senna and 15% for all others. Fresh infusions of quassia, calumba and senna should be boiled after preparation. Resistant organisms in calumba should be destroyed by boiling the aqueous extracts during the preparation of the concentrated infusion or by boiling the finished product.—K. Bullock and C. J. L. Elsdon, *Quart. J. Pharm.*, 1937, 413.

## Decocta.

Decoctions of drugs are usually prepared 5% (unless otherwise stated) by boiling the drug in coarse powder with distilled water for 10 minutes and straining. If necessary a few drops of chloroform will preserve fresh decoctions for a reasonable period of time. For various decoctions consult index.

Concentrated decoctions are prepared commercially as a general rule "1 to 7." They should contain at least 20% of alcohol as a preservative. Fresh decoctions are preferable.

## INSULINUM

B.P., Fr. Cx., P. Belg. IV.

Syn. ORDINARY INSULIN, REGULAR INSULIN, SOLUBLE INSULIN.  
[P1] "*Insulin.*"

[86] "*Insulin—specify the number of units as defined in the British Pharmacopœia contained in a specific quantity of the preparation.*"

[87] *Medicines made up ready for the internal treatment of human ailments containing insulin must be labelled with the words "Caution. It is dangerous to take this preparation except under medical supervision" instead of the word "Poison."*

The original patent (Br. Patent No. 203,778) was taken out by F. G. Banting, J. B. Collip and C. H. Best in the name of Toronto University, and the British rights were given to the Medical Research Council.

The Therapeutic Substances Act, 1925, and Regulations, 1931, control the manufacture under licence, standard, quality, containers, etc. Further Regulations, Part III, Sec. 9 (2), Aug. 1, 1931, provide for the addition of preservative to preparations like insulin, sealed in containers holding more than one dose.

The relation of the pancreas and diabetes was established by the experiments of Von Mering and Minkowski; extirpation of the pancreas in dogs was followed by persistent glycosuria. The pancreas consists of two types of tissue, the *acinar*, secreting the pancreatic juice (*external* secretion), which reaches the intestine through the pancreatic duct, and groups of cells, known as the "islets of Langerhans." The latter show pathological changes in varying degree in most patients dying of diabetes mellitus.

The islets of Langerhans were proved to contain a substance which lowers the blood sugar, and diminishes or abolishes excretion of sugar in the urine of diabetic dogs. Subsequently, by extracting foetal or adult normal pancreas with alcohol, an extract was made which caused a lowering of blood sugar, and of the glucose in the urine, when injected into a boy suffering from the disease. The alcohol evidently prevented the destruction of the principle by the digestive ferments.

On injection, it converts glucose into the active form, and if given at proper intervals blood sugar is maintained at normal level, and the urine remains free of sugar. Fat is completely oxidised. Acetone bodies disappear from the urine and diabetic acidosis and coma are prevented—a restoration to normal metabolism.

It is now becoming generally recognised that no tissue, other than that of the pancreas itself, contains insulin that can be extracted by the methods now available. Best and his co-workers have developed improved methods and repeated much of the earlier work on the extraction of insulin from various substances. Not only have they failed to find any evidence of the presence of insulin-like substances in various vegetables, but they have failed to find any extractable insulin in the blood, liver, spleen, kidney or muscle. Consequently, when an extract which acts like insulin is obtained from a tissue other than the pancreas, it is reasonably certain that the tissue concerned must be of pancreatic origin.—M. H. Power, R. W. Cragg and M. C. Lindem, *Proc. Mayo Clin.*, 1936, 101.

The old concept that every case of clinical diabetes was due to a dysfunction of the islands of Langerhans should be abandoned, and in its place should be substituted the broader concept that many, if not all, the characteristic features of clinical diabetes may be produced by agencies acting outside the pancreas. This concept does not in any way diminish the paramount importance of insulin in the regulation of carbohydrate, fat, and protein metabolism.—C. N. H. Long, *Proc. Mayo Clin.*, 1937, 288.

**Manufacture.** The method described in the *B.P.* involves the extraction of minced pancreas, which must be used fresh or kept frozen, with alcohol and hydrochloric acid. The filtrate is evaporated and treated with stronger alcohol, and the filtrate treated with dehydrated alcohol. The resulting precipitate is collected, dissolved in water and the active material separated by adjusting to the isoelectric point (which corresponds to a pH of between 5 and 6), or by treatment with trinitrophenol (picric acid). In the former case, the precipitate is dried and powdered. In the *picrate method* used in Gt. Britain (Brit. Patent 216,978, M.R.C. and H. W. Dudley), the precipitate is dissolved in an acidified aqueous-alcohol solvent, the insulin re-precipitated by pouring into acetone, and the precipitate dried.

[P1-87] **Crystalline Insulin.** The first crystalline insulin was obtained by Abel (*Proc. nat. Acad. Sci.*, 1926, 12, 132) by precipitating impurities from crude insulin in weak acetic acid solution by means of brucine, and then precipitating the insulin by the addition of N/6 pyridine. A potency of 40 units per mg. was claimed. Although other workers have claimed the isolation of crystals with activities very much greater than this—even up to 400 units per mg.—these results have not been confirmed. Culhane *et al.* (*Biochem. J.*, 1929, 397) found the activity of preparations obtained by Abel's and other methods to be 23 to 27 units per mg. Scott (*Biochem. J.*, 1934, 1532) showed that crystalline insulin contained zinc, and if electrodialysed to remove the metal it could not be crystallised. Crystallisation was found to be facilitated also by the presence of salts of other metals such as cadmium, nickel and cobalt. The ashes of crystalline insulins prepared with each of these metals contained a constant proportion of metal, and were proportional to the atomic weights of the metals each contained, thus indicating that the metal was in chemical combination in the crystals.

Ordinary commercial insulin was found to contain appreciable amounts of zinc, and in view of the action of zinc in slowing up the action of insulin, a plea is made for the standardisation of zinc-content of the commercial substance.—*Pharm. Weekblad.*, 1938, 1939, per *Analyst*, 1939, 129.

The administration of zinc to diabetic patients increases the blood sugar. Zinc also increases the antidiuretic activity of the pituitary posterior lobe and the secretory action of histamine, while with adrenaline it produces hyperglycæmia. It is essential therefore that the zinc content of commercial insulin should be standardised.—E. H. Vogelenzang and L. A. Hulst, *Acta med. Scand.*, 1939, 97, 307.

### **Chemical Composition and Stability.**

The empirical formula obtained for Abel's crystalline insulin is  $C_{45}H_{76}O_{17}N_{11}$ . Values for the molecular weight vary from about 10,000 to 37,000 according to the method, most results being

nearer the higher figure. Insulin obtained by precipitation at the isoelectric point is an amphoteric protein giving soluble salts with weak acids or alkalis. Strong acids precipitate the solutions and strong alkalis destroy the activity. It is most stable in acid solutions at low temperatures. Heating at  $80^{\circ}$  with 1% sodium chloride for 1 to  $1\frac{1}{2}$  hours causes coagulation. It is inactivated by proteolytic enzymes, e.g., trypsin, pepsin or papain, hence the ineffectiveness of insulin *per os*.

[P1-87] **Insulin in Solution (B.P.)** is obtained by dissolving the dry powder in water acidified to give a reaction between pH 3 and pH 4. *B.P. Add. I* requires that when insulin is prescribed, insulin in solution containing 20 units per ml. shall be dispensed unless some other strength, or insulin in tablets, is specified. It was originally required to contain an antiseptic at least as effective as 0.5% of phenol when distributed in containers holding more than one dose. *B.P. Add. I* makes the addition of an antiseptic optional, stating that "it is usual to add a sufficient proportion of some antiseptic to prevent the growth of any organism which may be accidentally introduced in the process of removing a portion of the contents of the container."

Solutions with pH 3 to 4 are themselves germicidal, but a slight increase of alkalinity destroys germicidal action and actually converts it into a culture medium if no preservative is present; the presence of the usual proportion of phenol suffices to keep it germicidal.—P. Hartley, *Lancet*, ii/1931, 584. Insulin and preservatives.—*Prescriber*, 1931, 406.

While insulin alone in normal dosage has no effect on the size of the heart-beat of the rabbit, and in 16 times the normal dosage the size of the beat decreases only very slightly, solutions containing cresol or phenol in the concentration in which they are normally used as preservatives cause a marked decrease in the size of the heart-beat. The alleged slowing of the heart-beat by insulin is due to the preservative used in commercial insulin solutions.—M. M. O. Barrie, *Quart. J. Pharm.*, 1936, 485.

[P1-87] **Insulin in Tablet Form (B.P.)** is obtained by compressing the dry powder mixed with a neutral diluent.

**Units.** A unit was originally taken as the amount of insulin which on subcutaneous injection lowers the percentage of blood sugar to 0.045 within 4 hours in a rabbit weighing about 2 kg. from which food has been withheld for 16 to 24 hours. Such insulin was first prepared so that 1 ml. contained 1 unit.

Subsequently the "clinical unit" was adopted. It was one-third the original Toronto unit, and was defined as one-third of the amount of material required to lower the blood sugar of a 2 kg. rabbit which has fasted for 24 hours from the normal level of 0.118% to 0.045% in 5 hours. In 1925 a unit based on a definite weight of a sample of crystalline insulin hydrochloride prepared by the National Institute for Medical Research was accepted internationally. Simultaneous determinations of the activity of this sample made by the National Institute, the Insulin Committee of the University of Toronto, and three other laboratories in the U.S.A. and in this country, varied only between 8.4 and 8.8 clinical units per mg. of the dried preparation. It was agreed to

regard this sample as containing 8 units. In 1935 the Permanent Commission on Biological Standardisation decided that henceforth *one international unit would be defined as the specific activity contained in  $\frac{1}{5}$  mg. of the new standard crystalline insulin preparation held by the Insulin Committee of Toronto University and the National Institute for Medical Research.* The unit of the B.P. is the activity contained in such an amount of this standard preparation as the M.R.C. may indicate to be equivalent to the international unit.

*Dose.*—(B.P.). By subcutaneous injection, 5 to 100 units.

Commence with 5 units twice a day—half an hour before breakfast and supper respectively. Most of the food should be taken in these two meals. If after 3 days of this dosage glycosuria still persists, the dose must be raised gradually, first to 10 and 10, and later 15 units or more, if required. On the 7th day test every 2 hours to get a further idea of the effect. By the 11th day all sugar and acetone may have disappeared from the urine, and the blood picture may have become normal. This may represent the permanent balance of diet and insulin, but more often the patient's pancreas improves so that by the 13th day 15 and 10 units are too much—12 and 8 units may suffice. Patient's tolerance may continue further, and still less insulin may be needed.

The most common error is to give too little insulin. Many doctors seem afraid to give doses of more than 10 units twice a day. The proper dose is that which the patient needs, and is always an individual one. Another difficulty is the necessity of varying dosage from time to time. No patient can continue on the same dose of insulin year in and year out, and if the necessary adjustments are not made, the patient will not be kept well. In added illness, especially a febrile one, the whole blood sugar picture moves upwards with the same dose of insulin, and ketosis might result and the patient be liable to go into diabetic coma. Therefore, in any added illness, it is essential to increase the insulin; this is most easily done by adding to the two daily doses a third in the middle of the day. When sickness and vomiting occur, if the patient can keep nothing down, it is a mistake to cut off the insulin entirely, but half the usual dose should be given, otherwise the blood sugar will rise.—R. D. Lawrence, *Brit. med. J.*, ii/1935, 1066.

*Technique of Injection.* Insulin is given subcutaneously (it may be given intravenously in coma), the skin having been previously sterilised. Wherever possible, patients should always be taught to give their own injections, the best sites being the front of the thighs, the abdomen and the lower part of the chest. Before breakfast the abdomen is a good site, and during the day the thigh in women and the skin below the knee in men are the most convenient. Pain is minimised by using a fine sharp needle and inserting at right-angles to the skin. It is less painful to inject the insulin quickly than slowly, and stinging is less likely to be felt if the site of injection is pinched as the insulin enters. The sting due to the acidity of the injection can be entirely prevented by mixing in the syringe one-quarter the volume of 6% sterile sodium bicarbonate. The alkali must not be introduced into the insulin bottle. To avoid local fatty atrophy the site of injections is changed every week or 10 days, and no two punctures should be made in exactly the same spot within 24 to 48 hours.

**Insulin Suppositories.** Tests with insulin suppositories made on rabbits and healthy human beings showed that the action of insulin introduced in this manner attains its maximum in 30 to 40 minutes and then subsides rapidly. Larger doses of insulin increase the intensity and duration of action. Suppositories of cocoa butter were ineffective, but a mixture of palmitic acid and cocoa butter in the proportion of 15 to 85 proved effective in preserving the efficacy of the insulin. The suppositories proved to be of clinical value.—B. Brahm, *Lancet*, i/1940, 829.

**Diet** must be strictly controlled, especially as regards carbohydrate content. It is obviously impossible to devise a standard diet, since the dietetic requirements must be varied to suit the individual case. According to Lawrence (*The Diabetic Life*, 1939) a satisfactory diabetic diet must be flexible and able to meet the following requirements: (1) It must supply the correct calorific requirements of the individual; (2) It must contain sufficient carbohydrate to prevent ketosis; (3) It must satisfy the patient in quantity and quality as far as possible; (4) It must be accurate, simple to calculate, and varied. In order to meet these requirements, Lawrence devised the "*Line-Ration*" diet scheme. This is presented in the form of a card (H. K. Lewis & Co. Ltd.) printed in two colours, the left-hand column in black giving a list of carbohydrate foods, and the right-hand column in red giving a list of protein and fat foods. One black portion contains 10 g. of carbohydrate and one red portion  $7\frac{1}{2}$  g. of protein and 9 g. of fat, and any black portion may be taken with any red portion to form one "line-ration." Equal numbers of black and red portions must usually be taken together, but the doctor at his discretion may prescribe more blacks than reds, especially for insulin cases. A suitable diet on which to begin insulin treatment is 15 blacks (150 g. of carbohydrate) and 10 reds, with most of the carbohydrate given at breakfast and the evening meal before which insulin is injected. In cases that do not require insulin a qualitative diet without preoccupation with total calories is sufficient, but with insulin cases it is always essential to give a regular fixed amount of carbohydrate to balance the correct dose of insulin.

**High Carbohydrate Diet.** Some workers have advocated diets containing a normal amount of carbohydrate, i.e., up to 350 or 400 g. per day, with a very low intake of proteins and fats. Rabinowitch has shown that by keeping the calories low, with very little fat, no more insulin is needed than with moderate carbohydrate and higher fat diets. Each patient is placed initially on a diet containing carbohydrate 133 : fat 61, further carbohydrate being added according to the patient's requirements in the form of Rabinowitch equivalents, which are as follows:—Any one of the following may be substituted for one slice of bread = 1 oz.: Two apples; two oranges; two grapefruit; three level dessertspoonfuls of cream of wheat; three level dessertspoonfuls of any one of the following: Wheat, barley, buckwheat, corn, cornmeal; two level dessertspoonfuls of rice; four heaped dessertspoonfuls of oatmeal; two heaped dessertspoonfuls of dried beans; two heaped dessertspoonfuls of dried whole peas; one cupful of toasted cornflakes;

one banana; one potato; five soda biscuits; four teaspoonfuls of jam or marmalade; three teaspoonfuls of sugar. Any one of the following may be substituted for one and one-half slices of bread =  $1\frac{1}{2}$  oz.: One shredded wheat; macaroni, eight strips, each being 8 inches long. (*N.B.* The cereals must be measured uncooked.)

Experience has shown that the assumption that increase in carbohydrate necessitates a proportional increase in insulin dosage is entirely false; although generally speaking it is true that 1 unit of insulin is required to metabolise 1 g. of glucose, this only holds good for the first 15 or 20 units; thereafter large amounts of carbohydrates may be added to the diet only with a relatively small increase of insulin. In America as much as 300 to 350 g. of carbohydrates have been included in the diabetic diet with striking results, though this often necessitates dosage of 100 units daily. Special diabetic foods are not only unnecessary but actually objectionable. High carbohydrate diet clears up the arteriosclerosis common in diabetics by reducing the blood pressure.—S. C. Dyke, *Lancet*, i/1932, 979.

A method of treatment, the fundamental idea of which is to give glucose covered by the necessary amount of insulin, as opposed to the general practice of insulin covered by glucose, *i.e.* give the maximum of sugar and the minimum of insulin. Blood-sugar estimations unnecessary. Diet chart given. Steady and automatic recovery of 41 cases at U.C.H.—H. P. Himsworth, *Lancet*, ii/1932, 165.

Obese patients do well on a low-calorie diet without insulin, with resulting weight reduction. If such patients are put on a diet that maintains their weight large doses of insulin are needed to control the diabetes.—F. Fetter *et al.*, *J. Amer. med. Sci.*, 1938, 195, 781.

**Hypoglycæmia: Effects of Excessive Dose.** There is a rapid fall of blood sugar to below normal following the injection of an overdose of insulin, a minimum being reached in 3 to 5 hours, the effect passing off in 5 to 12 hours according to the dose. The normal amount of blood sugar is 0.08 to 0.12% (fasting), or 0.13 to 0.17% after a carbohydrate meal. If the level falls to 0.06 to 0.07% symptoms of hypoglycæmia appear. In untreated diabetics who have become accustomed to a higher level, symptoms of hypoglycæmia may occur at higher levels.

The early symptoms are weakness, shakiness of the limbs, hunger, nervousness and fear. Mental confusion and diplopia may occur, with sweating and palpitation. Later, convulsions and coma may occur. The condition comes on gradually and is never dangerous if treated within 15 minutes of onset. Glucose or 2 lumps of ordinary sugar should be taken at once with water, and may be repeated in 15 minutes if needed. If coma occurs dextrose should be given intravenously (1 oz. in 20 to 50% solution), or sugar may be given orally, by stomach tube or *per rectum*. At the same time 1 ml. of 1 in 1000 adrenaline solution hypodermically or 1 ml. of pituitrin intramuscularly should be given.

**Suitability of the Case.** All cases, except those in whom immediate insulin treatment is indicated (*vide infra*), should be given a basal maintenance diet but not put to bed unless severe weakness is present.

The diet must be restricted as to carbohydrates, with a moderate amount of protein and fat. If at the end of the week's treatment on basal diet, the urine is not free of sugar, the patient requires

**insulin.** If the urine becomes sugar-free on this diet, insulin is unnecessary and the diet should be gradually increased, especially the carbohydrate, until it is adequate for the patient's ordinary duties.

There is no evidence as yet that the treatment is curative, but the disease can certainly be arrested and health restored by insulin. It is not recommended unless the treatment can be continued. The initial stages of treatment should be carried out in connection with facilities for blood and urine sugar estimations.

### *Patients Suitable for Immediate Treatment by Insulin.*

All child diabetics, except those of the mildest degree; patients at all ages who show under-nutrition, ketosis and dehydration; diabetics who are found to be suffering from an acute septic infection such as carbuncle or whitlow, or from a generalised acute infection such as influenza; diabetics on whom it is proposed to perform a surgical operation requiring a general anæsthetic; all patients in whom it is evident that coma is threatening.

There is considerable evidence that two types of diabetes can be differentiated on the basis of the speed with which they react to insulin. In one type, the *insulin-sensitive* type, insulin comes into action rapidly; in the other, the *insulin-insensitive* type, insulin comes into action slowly. The evidence is compatible with the suggestion that the disease in the sensitive type is due to deficiency of insulin, while in the insensitive type the disease is due not to a lack of insulin but to impairment of insulin action. At present, although there is evidence that the anterior pituitary gland may be responsible for the diabetes associated with hyperpituitarism the indictment of the pituitary gland as a primary factor in ordinary cases of human diabetes mellitus rests purely on analogy.—H. P. Himsworth, *Brit. med. J.*, i/1940, 719.

**Complications.** While there are no contraindications to the use of insulin certain complications arising during the treatment may necessitate modifications in dosage, etc.

**Acute infections,** such as influenza and pneumonia, cause a lowering of the sugar tolerance and an increased hyperglycæmia and ketosis, and necessitate a large increase in the dose of insulin, and the administration of sufficient fluids and dextrose.

**Local septic conditions,** such as boils, carbuncles, septic teeth, also give rise to increased hyperglycæmia and ketosis and call for additional carbohydrates in the diet and larger doses of insulin. Similar steps are necessary in the preparation of diabetic patients for emergency surgical operations.

**Pregnancy.** In the latter half of pregnancy hyperglycæmia is likely to occur, requiring the use of more insulin, while after childbirth hypoglycæmia is a probable emergency calling for a reduction of insulin.

**Heart disease.** In elderly subjects, or those suffering from myocardial disease, care must be taken to avoid too sudden a lowering of the blood sugar, and insulin dosage must be increased gradually. It must be used with great care in patients with a tendency to angina.

**Gangrene.** In elderly and arteriosclerotic patients great care must be taken to avoid gangrene of the feet, e.g., by the wearing



of warm socks and comfortable shoes. These patients should also be warned against cutting their corns.

**DIABETIC NEURITIS.** On the basis of the theory that most of the neuritic symptoms commonly met with in diabetics are due to the ischaemia of endarteritis, sodium chloride 15 to 90 g. daily by the mouth has been given in order to produce a vasodilating effect. All cases so treated obtained complete or marked relief of the symptoms.—H. R. Sandstead and A. J. Beams, *Arch. int. Med.*, 1938, 61, 371.

**Treatment of Coma.** Treat as for collapse, clear bowels with enema, or wash out the stomach and give as much fluid as possible orally, *per rectum*, or preferably intravenously if the patient cannot swallow. If not completely comatose, 2 drachm doses of sodium bicarbonate should be given 2-hourly to counteract acidosis, until the urine becomes alkaline. Give also insulin 40 or 50 units with dextrose 40 or 50 g. *per os*, repeating every 4 hours until the ketonuria disappears, reducing the insulin if the urinary sugar is decreased in amount. During this treatment give abundance of fluid by the mouth. If coma is complete, large quantities of injection of sodium chloride and acacia should be given intravenously, together with insulin and dextrose in quantities as above, the initial dose of each being given intravenously.

Severe cases of coma can only be effectively dealt with in hospital, and in these cases the practitioner is advised to give 50 units of insulin intravenously, with sugar and fluids if possible, and to pass on the case at once.

As a result of a study of 86 patients with diabetic acidosis, the following treatment is recommended:—(1) Immediate parenteral administration (one half intravenously, the remainder subcutaneously and intraperitoneally) of 60 ml. of a sixth-molar solution of racemic sodium lactate per kg. of body weight. (2) Immediate administration of 2 units of insulin per kg. of body weight. (3) Administration of 40 ml. of Ringer's solution per kg. of body weight as soon after the administration of sodium lactate as possible. (4) Repeated administration of insulin 6 hours later in a dose of 0.5 unit per kg. of body weight. (5) Transfusion of citrated whole blood or plasma (20 ml. per kg. of body weight) if oedema due to reduced plasma protein develops.—A. F. Hartmann and M. Morton, *Arch. intern. Med.*, 1935, 413.

Administration of vitamins B<sub>1</sub> and B<sub>2</sub> has been found successful in interrupting coma in non-reversible cases of insulin shock. Patients who previously had awakened with 33% dextrose solution in quantities of 70 to 140 ml. and then failed to do so with 50% dextrose solution (400 ml.) were roused in 20 or 30 minutes by the administration of 800 units of "Betaxan" or yeast emulsion. In other cases it was possible to lessen the hypoglycaemic state before the administration of dextrose.—R. Freudenberg, *Wien. klin. Wschr.*, i/1937, 535.

#### Rules for Distinguishing Insulin Coma from Diabetic Coma:

**IN INSULIN COMA:**—(1) Skin usually very white, but may be normal in colour. (2) Breath does not smell of acetone. (3) Respiration shallow. (4) Eyeball tension normal or raised. (5) Urine usually sugar-free, but may contain sugar if bladder has not been emptied for some hours. (6) Urine need not contain acetoacetic acid to Rothera's test, but may do so if bladder has not been emptied for some hours. (7) Blood sugar below 70 mg. per 100 ml. and may be as low as 40 mg. per 100 ml. **IN DIABETIC COMA:**—(1) Skin usually flushed. (2) Breath smells of acetone. (3) Respirations deep. (4) Eyeball tension much lower than usual. (5) Urine always contains large amounts of sugar. (6) Urine always contains large amounts of acetoacetic acid. (7) Blood sugar is over 200 mg. per 100 ml., and may be up to 500 to 800 mg. per 100 ml.—G. Graham, *Med. Pr.*, 1934 (Symposium No. 1).

**Testing Expired Air for Acetone.** Moisten a watch-glass with Scott-Wilson reagent and hold close to patient's mouth and nose for 2 or more minutes. Acetone reaction shown by clouding of the reagent. Of practical value in the differential diagnosis of the unconscious state, e.g., diabetic coma.

**Other Uses of Insulin.** Apart from its use in the treatment of diabetes mellitus, insulin is of great value in many cases of non-diabetic malnutrition and during convalescence after serious illness. In these conditions it has a marked tonic action and leads to a gain in weight and to an improvement in the general health and mental outlook. The insulin is given subcutaneously two or three times a day before meals, the treatment being continued for four or five weeks. Dosage varies with the individual case and according to whether the patient is in hospital or is ambulatory. In the former case an initial dosage of 5 units three times daily is given, increased by 5 units daily up to 20 or 30 units three times daily; in ambulatory patients the dosage must be smaller. This tonic action of insulin has also been found of value in the treatment of pulmonary tuberculosis; it is in no sense a causal treatment, but it improves the general health and well-being of the patient and increases his resistance.

During recent years hypoglycæmic shock therapy has been used with success in the treatment of schizophrenia. Treatment consists in the administration of insulin in increasing doses until the "shock phase" is reached. Commencing with 10 to 20 units, the dose is raised by 5 to 10 units every day until a state of hypoglycæmia results; in some cases, doses as high as 190 units have been given. Remarkable results have been obtained, but the treatment is dangerous and should only be carried out in an adequately equipped mental hospital, and it is essential to have immediately available suitable solutions of dextrose for intravenous injection to interrupt the hypoglycæmic state.

In addition to its parenteral uses, insulin has been employed to some extent locally as a stimulant dressing to chronic ulcers, septic abrasions and bed sores. Good results have been claimed, but this form of therapy has not met with any wide measure of support.

#### GENERAL REFERENCES

**DIABETES.** In 1922 the average life of a diabetic was 6 years; to-day patients who started treatment with insulin on its introduction 9 years ago are still alive, and a growing percentage outlive their life expectancy.—E. P. Joslin, *J. Amer. med. Ass.*, ii/1931, 595.

The answer to the question "Will insulin cure me?" is that insulin cures diabetes as food cures hunger. Hunger recurs after a few hours, and the need for insulin also recurs. A wooden leg enables a lame man to walk, but not to grow a new leg. When the artificial leg is removed he falls to the ground. But the disease can certainly be arrested and health restored by insulin. It is wrong and untrue to offer more.—R. D. Lawrence, *The Diabetic Life* (1939).

Prognosis of diabetes in children. "Before the discovery of insulin the mortality of diabetes in childhood was nearly 100%, and to-day diabetes as a cause of death in the young has disappeared nearly to the vanishing point." (Priscilla White, *Diabetes in Childhood*.) No gloomy prognosis is justified in this insulin era, but continuous care and treatment are certainly necessary, and in practically every case insulin injections. A cure is not possible, but growth and development proceed normally and average weight is maintained.—R. D. Lawrence, *Lancet*, i/1934, 807. See also L. Cole, *ibid.*, 947, 998.

**DYSMENORRHOEA.** In a group of twelve patients, all nulliparas, suffering from primary or essential dysmenorrhœa, ten received practically total relief from menstrual pain by using insulin (from 7 to 10 units daily) from 3 to 7 days before or during the period. One patient obtained relief in one period with one type of insulin and no relief during another period with another type of insulin. Another patient was only partially relieved.—A. Altschul, *J. Amer. med. Ass.*, i/1936, 1383.

The cramp-like pains of dysmenorrhœa may be relieved by a single injection of 5 to 7 units of insulin with a supply of carbohydrate to counteract the anti-diabetogenic effect produced by the insulin.—E. W. Schrick, *Amer. J. Obstet. Gynec.*, May, 1939.

**HEART DISEASE.** Of value in congestive heart failure, especially in arterial and coronary syndromes. Six cases of intractable angina pectoris successfully treated with 5 units of insulin before breakfast and before the evening meal, each dose followed by 30 g. of dextrose taken with the meal, the patients continuing to take any remedies they had previously been taking. Treatment continued for from 2 to 17 weeks.—K. Shirley Smith, *Brit. med. J.*, i/1933, 696.

**PREGNANCY, VOMITING OF.** Combined use of dextrose intravenously with insulin hypodermically—about 2 g. dextrose in 10% solution to each unit of insulin—of value in excessive vomiting of pregnancy and in eclampsia.—*J. Amer. med. Ass.*, i/1926, 557.

**PULMONARY TUBERCULOSIS.** Increased appetite and progressive increase in weight with subcutaneous injections of 5 units before meals.—Morin and Bouessée (Leysin), per *Prescriber*, 1928, 187.

While insulin is not to be regarded as a cure for tuberculosis, and its systematic use in all cases is to be discouraged, it should be generally recognised as an important therapeutic measure in restoring normal appetite and digestion, and in combating loss of weight and resistance. Its use should be avoided when there is fever, active pulmonary disease, hæmoptysis, marked hypotension, and when severe reaction follows the injections. Begin with 5 units hypodermically 20 minutes before the principal meal, and follow three hours later with a glass of milk or a tablespoonful of glucose. The injection of 5 units is continued daily for the first week and increased by 5 units weekly, so that by the sixth week 30 units daily are given (15 before lunch and 15 before dinner), with milk or glucose three hours after lunch or dinner. This maximum daily dose is repeated for four or more weeks, and the whole course can be repeated at intervals, though in many cases the effects of insulin are maintained after the first course has been discontinued.—P. Elman, *Practitioner*, i/1937, 613.

**SCHIZOPHRENIA.** Treated by hypoglycæmic shock, produced by means of huge doses of insulin. Method is dangerous, but 70% of full remissions claimed, although these were all early cases.—*Lancet*, i/1936, 1018.

Shock treatment of schizophrenia.—G. W. B. James and Co-workers, *Lancet*, i/1937, 1101.

In 34 cases treated by insulin shock eight obtained complete remission, i.e., disappearance of every abnormality indicative of schizophrenia, and in 15 there was improvement. An undesirable effect of the treatment is its diminution of the patient's resistance to infections, and it was often necessary to discontinue the treatment because of sore throats or boils.—E. Küppers, *Dtsch. med. Wschr.*, 1937, 377.

One year's experience leads to the conclusion that the insulin-hypoglycæmia treatment is a promising therapeutic approach to the schizophrenic problem, but since experience plays such a large role in determining efficacy and forestalling danger the method should not be attempted save in an adequately equipped mental hospital or under the immediate supervision of a well-trained psychiatrist, who should also be capable of meeting the emergencies that may arise.—E. Cameron and R. G. Hoskins, *J. Amer. med. Ass.*, ii/1937, 1246; see also C. A. Rymer *et al.*, *ibid.*, 1249.

For the interruption of therapeutic hypoglycæmic coma the most satisfactory nasal feed is 600 ml. of 33% sugared tea. For its interruption by intravenous injection 100 ml. of 33% glucose is necessary to ensure a normal blood-sugar for a further half-hour, independent of absorption from the stomach. To ensure a normal blood-sugar for an hour after interruption by intravenous injection when absorption from the stomach cannot be relied on 250 ml. of 33% glucose should be given. For cases of "irreversible" coma or with persistent vomiting

during recovery an immediate intravenous injection of 250 ml. of 33% glucose should be given.—R. Fraser and D. A. Stanley, *Lancet*, i/1939, 140.

**TONIC ACTION.** Of value for increasing the weight of persistently thin people, the dose being 10 units 3 times a day about 20 to 30 minutes before meal, accompanied by a liberal, unmeasured diet. Treatment continued for several weeks. Patients gained weight rapidly and immediately, the increase tending to become less marked as weight approached normal standard, and the weight remaining constant, or continuing to increase, on omission of insulin. Local skin hypersensitiveness occurs in some cases, but hypoglycæmic reactions rare. Insulin serves as an admirable tonic both physiologically or psychologically.—H. Blotner, *J. Amer. med. Ass.*, i/1933, 91.

The majority of 100 patients so treated maintained the added weight and the improved general condition for as long as six years after discontinuing insulin and a few continued to gain. Insulin induced at least a temporary improvement even in those who did not retain the weight, and in a number of cases various complicating factors were adequate causes for the loss of the gained weight.—H. Blotner, *New Engl. J. Med.*, i/1938, 371; *Med. Pr.*, i/1939, 277.

**VARICOSE ULCERS.** Insulin injected, and locally, found of value.—*Pharm. J.*, ii/1925, 180. Ulcers of leg well treated.—*Brit. med. J. Epit.*, ii/1925, 10.

Several of 30 cases are described in which insulin, either in aqueous solution or as an ointment, was applied in chronic septic cases such as varicose ulcers and septic abrasions. In many of the cases treated other treatments had proved ineffective, while relief after insulin applications was very prompt.—per *Chem. & Drugg.*, i/1939, 193.

In general it may be concluded that insulin is no more satisfactory as an external dressing than a similar solution of tricresol containing no insulin.—A. R. Hunter, *Brit. med. J.*, i/1939, 773.

Insulin applied locally (12 units twice a day in the form of a wet dressing) completely healed a resistant non-diabetic ulcer of 5 months' standing in 10 days.—Per *J. Amer. med. Ass.*, ii/1925, 473.

## PROTAMINE INSULIN COMPOUNDS

One of the chief drawbacks to the use of ordinary or soluble insulin is the transitory nature of its action, which necessitates the administration of two, three or even four injections daily. In 1936 Hagedorn and his Danish colleagues introduced a relatively insoluble compound, protamine insulinate, which was absorbed more slowly than ordinary insulin and thus had a more prolonged effect on the blood sugar. This new compound, though representing an important advance in insulin therapy, still suffered from certain disadvantages, one being its relative instability (it is not guaranteed to remain active for more than a few weeks) and another that even with very large doses it is seldom possible to control severe diabetes with only one dose a day.

D. A. Scott of Toronto, who had already shown that zinc is a constituent of crystalline insulin (see p. 625) and that the effect of insulin is modified by its presence, found that protamine insulinate when freed from such traces of zinc was no more prolonged in action than ordinary insulin. By the addition of small traces of zinc to protamine insulinate and the adjustment of the pH to 7.2 he produced a protamine zinc insulin compound which has a much more prolonged action than protamine insulinate and much greater chemical stability. Although, in practice, it has not been found possible to employ protamine zinc insulin in place of ordinary insulin in every case of diabetes requiring insulin treatment, its use, either alone or in conjunction with ordinary

insulin, is becoming increasingly recognised as a procedure of established therapeutic value.

[P1·87] **Protamine Insulinate.** *Syn. and Prop. Name.* PROTAMINE INSULIN, INSULIN-P, DELAY INSULIN, LEO INSULIN RETARD (*Nordisk Insulin Laboratorium, Copenhagen; Bencard, London*).

This is a compound obtained by combining insulin hydrochloride with a protamine derived from the sperm of a species of trout, *Salmo iridius*. Owing to its relative instability in a buffered solution it is issued in two bottles, one containing 5 ml. of soluble insulin (40 units per ml.) and the protamine in acid solution, and the other a 1% solution of sodium phosphate. In use, 1 ml. of the sodium phosphate solution is injected into the bottle of protamine insulinate. This produces a precipitated insoluble compound, which must be used within a month. The mixture must be vigorously shaken on every occasion before use.

Protamine insulinate has a more prolonged effect than ordinary insulin, its action lasting for about 12 hours, so that it is possible to ensure a normal fasting blood sugar concentration in the morning by giving an adequate dose in the evening. Except in fairly mild cases, however, it is usually necessary to give two injections a day, and Hagedorn himself states that the best results are usually obtained by giving ordinary insulin in the morning and protamine insulinate at night. In some cases successful results may be obtained by giving two nearly equal doses of protamine insulinate before breakfast and before the evening meal and spreading the day's carbohydrate equally over four meals a day.

*For references to original papers on Protamine Insulinate see Vol. I, 21st Edn.*

[P1·87] **Protamine Zinc Insulin.** *Syn.* ZINC PROTAMINE INSULIN, PROTAMINE INSULIN (WITH ZINC) SUSPENSION.

*Dose.*—As initial dose, about two-thirds the number of units of ordinary insulin necessary daily to maintain the patient sugar-free. It is usual to administer sufficient to maintain the patient on a single daily dose, i.e., between 20 and 60 units given subcutaneously about one hour before breakfast.

Prepared by the addition of a small trace of zinc to protamine insulin and adjusted to a pH of 7·2 by the addition of solution of sodium phosphate. Protamine zinc insulin occurs in the form of a suspension, and the container should be shaken on each occasion before use. In cases where ordinary insulin is also required it may be taken up in the same syringe and injected with the protamine zinc insulin; the ordinary insulin should be drawn into the syringe first.

*Method of Administration.* Protamine zinc insulin may be used either alone or in conjunction with ordinary insulin. According to Lawrence, in mild insulin cases requiring 10 to 30 units a day, who previously had two doses of 5 to 15 units of ordinary insulin, protamine zinc insulin acts admirably when given in one

dose before breakfast, while severe cases can usually be satisfactorily controlled by the addition of ordinary insulin before breakfast; in the most severe cases an extra dose of ordinary insulin is required in the afternoon or evening. Although Lawrence now treats all new cases, initially, with protamine zinc insulin, supplemented if necessary with ordinary insulin, he does not recommend changing cases who are in good health, contented, and well controlled by two doses of ordinary insulin.

With regard to diet, most patients on protamine zinc insulin manage well on 150 g. of carbohydrate daily, which may suitably be distributed as follows: Breakfast 30 g., lunch 30 g., tea 30 g., dinner 40 g., bedtime 20 g. Where ordinary insulin is given in addition it is advisable to supply additional carbohydrate at breakfast time. It is important to remember that regularity in the time of meals is essential, since delay in the taking of a meal may precipitate an attack of hypoglycæmia.

It is difficult to devise rigid rules for changing from ordinary insulin to protamine zinc insulin, but the following scheme outlined by Chase (*Canad. med. Ass. J.*, ii/1938, 267) may be found of value. Add the total number of units the patient is taking in 24 hours. If the total is under 40 add 5 to obtain the initial dose of protamine zinc insulin and in addition give 5 units of ordinary insulin for 5 days before breakfast. As soon as all tests for 24 hours are sugar-free the dose of protamine zinc insulin is reduced 5 units a day, and when the dose gets below 20 units it is reduced 2 units a day. If the total units of ordinary insulin taken in 24 hours are more than 40 add 10 to obtain the initial dose of protamine zinc insulin and in addition give 10 units of ordinary insulin before breakfast. The protamine zinc insulin is reduced 10 units a day as soon as all tests are sugar-free.

**ADVANTAGES AND DISADVANTAGES.** Although protamine zinc insulin possesses certain obvious advantages over ordinary insulin, in particular its greatly prolonged action, resulting in the complete absence of ketosis throughout the twenty-four hours, and the practicability in many cases of a single daily injection, it also possesses certain disadvantages which necessitate caution in its use; of these the most important are the late and insidious hypoglycæmia and the lack of uniformity in action owing to its variation in rate of absorption. For the treatment of diabetic coma protamine zinc insulin is not sufficiently rapid in action and cannot replace ordinary insulin, though it may be given as an adjuvant.

At present zinc protamine insulin is the only insulin, besides soluble insulin, generally used in this country, the use of Hagedorn's original protamine insulin having been largely discontinued. During the past year 150 out-patient diabetics have been converted from soluble to zinc protamine insulin alone or to zinc protamine insulin with some soluble insulin in addition. As the result of observations on these patients it would seem to be usually unnecessary to hospitalise patients during the process of conversion, except in the case of those who originally required very large doses of soluble insulin. 45% of the patients had no recurrence of glycosuria during the transition period, 33% had an insignificant and very temporary return, and in only 22% was the return of glycosuria at all severe or prolonged. The average dose of zinc protamine insulin necessary

for stabilisation over a series of 102 cases was 26.7 units, in contrast to an average total daily dose of 30.8 units of soluble insulin. It is necessary to see out-patients at frequent intervals while the conversion is being carried out. In individual cases the previous total daily dose gives only a rough estimate of the amount of zinc protamine insulin which will eventually be required. Where the total daily dose of soluble insulin was small—25 units or less—the patient can be started with the same dose of zinc protamine insulin, to be altered as required later. Where a larger total dose of soluble insulin was needed it is better to start with three-quarters of the dose in the form of zinc protamine insulin, the other quarter being given as soluble insulin—this latter can be abandoned in the course of a few days. Approximately 77% of the cases were able to do without soluble insulin at all relying entirely on a single dose of zinc protamine insulin; in the remainder a small dose of soluble insulin had to be continued to deal with the hyperglycaemia induced by the breakfast carbohydrate, the dose of zinc protamine insulin being appropriately reduced to avoid hypoglycaemic symptoms in the evening or at night. The insulin is given as early as possible before breakfast. Where soluble insulin has to be given in addition it is injected first. The syringe is then disconnected from the needle, a new needle is then fitted on to the syringe and the dose of zinc protamine insulin is sucked in. The syringe is then again connected to the original needle and the zinc protamine insulin injected. Thus the two forms of insulin are not mixed in the syringe and the patient only has one prick with the needle. A new case of diabetes can be started straight away on zinc protamine insulin alone, provided the case is a moderate one. 10 or 12 units can be given to begin with and dose gradually increased by 4 units at a time, allowing four days to elapse between each increase. If the new case, however, is a severe one soluble insulin is used entirely at first, and conversion to zinc protamine insulin alone or with soluble insulin carried out when the patient is stabilised. Hypoglycaemic reactions are less numerous and generally less frequently severe with zinc protamine insulin than with soluble insulin, but when severe reactions do occur they are more severe and more difficult to treat. Patients should be warned that the symptomatology of the zinc protamine insulin reactions differs from that of soluble insulin. In the latter, sweating, palpitations and tremors are characteristic but in the former general malaise, nausea and vomiting and particularly headache are the most frequent. Children respond extremely well to zinc protamine insulin, and the advantage of having to give only one injection daily makes it particularly suitable in such cases.—D. M. Dunlop, *Edinb. med. J. (Trans. Medico-Chirurg. Soc. Edinb.)*, 1938, 194.

In adjusting the dose, increases should not be made oftener than every 2 to 4 days and then only by 5 units or less at a time. Patients who get reactions must be observed over a prolonged period after the administration of glucose, since the administrations may need to be repeated several times in succession.—C. W. Howe and D. W. J. Bell, *New Engl. J. Med.*, i/1937, 1095.

Observations of the effect of protamine zinc insulin on the glycosuria of diabetics receiving constant diets (usually in three half-hourly feedings) indicate that a large and possibly maximal insulin effect is exerted on carbohydrate metabolism within 3 to 6 hours of the injection, and that the total duration of effect of doses lying between 15 and 100 units is 15 to 60 hours.—R. S. Aitken, *Lancet*, ii/1938, 788.

Ordinary insulin is much more potent when given in conjunction with protamine zinc insulin than when given alone, and in such circumstances the initial doses of ordinary insulin should be limited to 4 or 6 units and raised by 2 unit increases to about 12 to 14 units once or twice a day, before breakfast, dinner, or both, as the usual safe upper limit.—H. O. Mosenthal and M. F. Mark, *J. Amer. med. Ass.*, ii/1939, 17.

Allergic reactions are decidedly more common with protamine insulin than with standard insulin, and annoying local reactions may occur at the site of injection of more than 1 ml. of protamine insulin, in the form of hard, firm, inelastic nodules which persist for two or three days and are gradually absorbed without discoloration.—H. M. Feinblatt, *J. Lab. clin. Med.*, 1939, 24, 340.

Local reactions at the site of injections of protamine zinc insulin are sufficiently frequent to assume clinical importance. It is suggested that the insulin sensitivity is induced as the result of the more prolonged action of the antigen (insulin) in the course of its slower absorption from a precipitated state.—R. A. Kern and R. H. Langner, *J. Amer. med. Ass.*, ii/1939, 198.

It is the practitioner's insulin for choice, but in severe cases it is rarely possible

to keep the urine constantly sugar-free without risk of hypoglycæmia. The dose should be reduced if all the urine tests are free for even one day, and certainly for two days, otherwise hypoglycæmia is sure to occur. These patients ought to pass some sugar after breakfast and usually some after supper. If a patient never passes sugar after supper or before breakfast the basal dose is too high and should be reduced, perhaps by 4 units; if he never passes sugar after breakfast the soluble insulin should be reduced.—R. D. Lawrence, *Brit. med. J.*, i/1939, 1077.

It is more economical and ensures more accurate balancing to give soluble insulin and zinc protamine insulin in separate injections. If drawn into one syringe they must not be allowed to mix.—G. M. Wauchope, *Lancet*, i/1940, 962.

### OTHER INSULIN PREPARATIONS

**Alum-precipitated Insulin** has been recommended as less likely than the zinc compound to cause delayed and serious hypoglycæmic reactions. It can be given in one single dose and its action begins within two hours, thus obviating a supplementary injection of ordinary insulin to cover the after-breakfast rise of blood-sugar, while its effects wear off in twenty-four hours, thus eliminating the fear of a delayed reaction.—L. Rosenthal *et al.*, *Amer. J. med. Sci.*, 1939, 198, 98.

**Hexamine Insulin.** A compound of hexamine insulin has been prepared, using 0.25 g. of hexamine to 1000 units of insulin. This gives a very fine precipitate which can be dissolved on either the acid or the alkaline side and reprecipitates at the pH of the body tissues. This preparation can be buffered and is non-irritating. The alkaline-buffered solution is as stable as protamine insulin and, when cleared, can be used in any concentration. Fourteen severe cases of juvenile diabetes, including patients treated with ordinary, crystalline, and protamine insulin, were treated with a single daily dose of hexamine insulin. It was found that a single dose of hexamine insulin may be substituted for 2 to 4 divided doses of ordinary insulin, producing a similar blood-sugar curve but with decided constriction in the range fluctuations of blood-sugar. The absence of ketonuria was as striking with hexamine insulin as with protamine insulin, and it has a specific effect in decreasing polyuria in those patients who complained of it both with ordinary and with protamine insulin. Shocks caused by hexamine insulin respond immediately to the ingestion of small amounts of carbohydrates.—H. M. Feinblatt, *J. Lab. clin. Med.*, 1939, 24, 337.

**Insulin-Tannic-Acid-Zinc-Suspension.** A mixture consisting of insulin and tannic acid in the proportion of 1 to 2, with the addition of zinc, 1 g. to 500 units of insulin, may be used successfully in diabetic patients in place of protamine-insulin-zinc, and in the same dosage in patients who show no cutaneous reactions, but a trial injection is first necessary since it is liable to produce irritant skin reactions in some patients.—C. N. Jenkinson and K. J. G. Milne, *Brit. med. J.*, i/1938, 380.

The addition of tannic acid prolongs the hypoglycæmic action of insulin, and the action is still further prolonged by the addition of zinc to the tannic acid-insulin complex. If the ratio of tannic acid to insulin is 2 : 1 the tannic acid-insulin-zinc suspension produces a hypoglycæmia as prolonged as that produced by protamine-insulin-zinc suspensions. With this ratio of tannic acid to insulin 99 to 100% of the insulin is precipitated. Clinical trial is suggested of a preparation of tannic acid-insulin-zinc containing tannic acid-insulin in the ratio of 2 : 1, and 1 mg. of zinc to each 500 units of insulin.—W. A. Broom and E. M. Bavin, *Quart. J. Pharm.*, 1937, 334.

**Pectin-Insulin.** A pectin-insulin preparation, which has been given the name "decurvon," has been found to exert a protracted action. The best results are obtained with solutions of 4 to 5% of pectin, with a pH of 4.0 to 4.4, in which the insulin is dissolved. Absorption of the insulin sets in immediately after injection and is regular and prolonged. In healthy fasting men the blood-sugar decreases for at least three hours after the injection of 10 u. of decurvon and does not begin to rise until after six hours. In contrast with depot insulin decurvon can also be injected intravenously.—B. Brahn, *Lancet*, i/1940, 1078.

### PREPARATIONS FOR ORAL USE IN DIABETES

In view of the obvious disadvantages of the administration of insulin by injection, numerous attempts have been made to produce compounds which



would withstand the action of the digestive enzymes and thus be active when given orally. Although success has been claimed with a variety of compounds, none of these claims has so far been substantiated. Among the compounds which have been tried are compounds or mixtures of insulin with saponin, bile acids, and blood serum.

Substances or preparations for oral use other than insulin have been advocated from time to time in the treatment of diabetes, but in no case can they be regarded as complete substitutes.

[P1-81] **Synthalin** (*Schering, London*).  $C_{12}H_{22}N_4Cl_2 = 329.32$ .

*Dose*.—0.01 to 0.03 g. daily. Issued in tablets containing 0.01 g.

Synthalin is decamethylene-guanidine dihydrochloride. It is a white, odourless crystalline powder melting at  $193^\circ$ ; soluble in water.

*Uses*. Synthalin reduces glycosuria and blood sugar when given orally and is used in mild cases of diabetes mellitus or in conjunction with insulin. Treatment should commence by rendering the patient sugar-free by diet, and then giving carbohydrate so that excretion of sugar in the urine is 25 to 40 g. per day.

From the clinical point of view, it can reduce acetone and sugar excretion by some 10 to 30 g. a day, but it cannot replace insulin in severe cases and does not have the same effect as insulin in milder cases of increasing strength and energy. It has the great disadvantage of causing toxic symptoms in many people, general depression, gastro-intestinal disturbances, nausea, vomiting and diarrhoea. Its continued administration must be stopped after weeks or months, and in the interval recourse must be had to insulin. One must hesitate to use a drug whose action is a toxic one and whose effect in checking sugar excretion is brought about by a pathological depression of metabolism unlike the physiological action of insulin therapy. Considered opinion in this country has always been against it. An oral preparation is an ideal which unfortunately has not yet been achieved.—R. D. Lawrence, *The Diabetic Life*, 1939.

[P1-81] **Synthalin B** (*Schering, London*) is dodecarnethylene-diguanidine hydrochloride and possesses similar properties to Synthalin. It is milder in action but better tolerated, and is given in doses of 0.005 to 0.01 mg. daily.

[P1-81] **Anticomman** (*Riddell Products, London*). Decamethylene-diguanide bitartrate, pancreas ferment (lipase), sodium phosphate. Tablets, each containing 3.6 mg. of decamethylene-diguanide, for the oral treatment of diabetes: in severe cases as adjuvant to insulin injections.

On oral administration (in rabbits) 50 mg. of decamethylenediguanidine bitartrate per kilo are lethal. 40 mg. produce a slight hypoglycæmia, smaller doses have no effect. On subcutaneous injection doses over 6 mg. per kilo are effective in producing hypoglycæmia but are fatal. The effect of the drug is to produce tubular nephritis, similar to that obtained in mercuric poisoning. From these results the drug cannot be expected to be of value in clinical cases.—P. L. Ewing and H. Segenreich, *J. Lab. clin. Med.*, 1936, 181.

**Galega**. Doses of 80 to 100 drops twice daily by mouth of a liquid extract of galega, standardised to contain 3% of the alkaloid, galegine, of value in diabetes. Its action resembles that of Synthalin (*vide antea*), and it is quite harmless and without contraindications. It is active both in mild and in moderately severe diabetes, and is especially useful in insulin-resistant cases.—G. Parturier and G. Hougnot, *Pr. méd.*, 1935, 258.

**Galegine**, the alkaloid of *Galega Officinalis*, has a similar constitution to Synthalin, and has been used for reducing blood sugar, replacing 20 to 30 insulin units. No secondary effects observed.—*Pharm. J.*, ii/1927, 563.

**Glucosone**, or aldofructose (one of the oxidation products of dextrose or fructose) has similar properties to insulin and is given by the mouth.—P. T. Herring, *Lancet*, i/1927, 1000.

For a full account of the chemistry and physiology of insulin with several hundred references to original papers see "Insulin, its Production, Purification and Physiological Action," by D. Hill and F. Howitt (1936). For the treatment of diabetes, see "The Diabetic Life," by R. D. Lawrence (1939).

## IODOFORMUM

*B.P., U.S.P. XI, Fr. Cx., P. Jap. V, P. Helv. V, P. Dan.*

$\text{CHI}_3 = 393.8.$

*Syn. TRI-iodomethane.*

*Dose.*— $\frac{1}{2}$  to 3 grains (0.03 to 0.2 g.).

Yellow crystals or unctuous powder with characteristic odour. Contains 96.7% of I. M.p.  $120^\circ$  to  $122^\circ$ .

To cover its odour it may be mixed with coumarin, 1 in 50, or with menthol, phenol, thymol, oils of anise, eucalyptus, geranium, peppermint, rosemary or sassafras, about 1 or 2%.

To remove the smell from the hands, utensils, etc., rub with a little crushed linseed and wash afterwards.

**Soluble** 1 in 8 of ether, 1 in 10 of ether (sp. gr. 0.735), 1 in 10 of chloroform, 1 in 7.5 of benzene, 1 in 100 of 90% alcohol, 1 in 14 of eucalyptus oil, 1 in 10 of collodion, 1 in 60 of soft paraffin and oil of almonds, and about 1 in 30 of olive oil. Almost insoluble in water, but soluble 1 in 10 of Rubini's solution of camphor, which disguises its odour.

**Antidotes.** Give sodium bicarbonate freely, in plenty of water. Keep patient warm and give brandy,  $\frac{1}{2}$  oz., or aromatic spirit of ammonia,  $\frac{1}{2}$  dr., in water. Bromides, in 60 gr. doses, if necessary.

**Uses.** Taken internally iodoform is gradually absorbed and is partially decomposed, liberating inorganic iodine. It has been used internally in syphilis, goitre and phthisis, originally with the idea that it would act as an iodide, but it is only partly broken up and its action is quite different from the inorganic iodides. Nevertheless, it is stated to be of value in early pulmonary tuberculosis, beginning with  $\frac{1}{2}$  or  $\frac{1}{4}$  gr. after meals thrice daily and increased by  $\frac{1}{4}$  or  $\frac{1}{2}$  gr. weekly or fortnightly to the point of tolerance, the treatment being continued with intermissions for 6 months or a year. It has also been employed hypodermically or intramuscularly in various forms of pulmonary affection and in tuberculosis of the bones and joints, employing a dose of 0.5 to 2 ml. of a 1% solution in oil once or twice daily.

Externally it is employed for its antiseptic action and to promote granulation; it exerts a marked anæsthetic action on mucous membranes and raw surfaces. Its chief value is as an external application to painful ulcers and as an antiseptic dressing to wounds, especially in the form of a paste with bismuth subnitrate and liquid paraffin (*see B.I.P.P.*, p. 314). It is stated to be almost specific in the local treatment of chancroid and syphilitic ulcers. It is also of undoubted value as a topical application to tuberculous abscesses and especially in tuberculous laryngitis with ulceration, when it may be used as an insufflation, 2 to 5 gr. of undiluted powder (well triturated), or with equal parts of starch powder or boric acid.

**Caution.** Many cases of poisoning have been reported from its free use as a surgical antiseptic, and it is advisable that in ordinary cases not more than 2 g. should be used as a wound dressing. Apart from this some people have a marked idiosyncrasy to iodoform, and its use even in small doses by local application may give rise to an erythematous rash.

**AMEBIASIS.** Nine cases of subacute and chronic amoebic colitis satisfactorily treated. Patient kept in bed on a fluid or very light diet, and after a preliminary purge (magnesium sulphate 15 g.), iodoform is given in the form of keratinised capsules containing 0.05 g., 1 or 2 capsules 3 or 4 times a day for 12 to 15 days. The treatment may be repeated after an interval of 1 week. Toxic symptoms not noted except in one patient who complained of vertigo. No rash noted.—Sir A. Castellani, *J. trop. Med. (Hyg.)*, 1935, 268.

Eight cases of amoebic colitis treated with excellent results by administration of iodoform in keratinised capsules containing 0.05 g. for each dose. Begin with an initial daily dose of 0.05 to 0.10 to 0.15 g., reaching a maximum daily dose of 0.20 to 0.30 g., the treatment lasting about 12 to 20 days. There were no symptoms of intolerance and no rash.—C. Scotti, *J. trop. Med. (Hyg.)*, 1937, 174.

**LEPROUS ULCERS** well treated by application of 16 gr. to 1 oz. of acetone for small ulcers and 10% iodoform in eucalyptus oil for large and sloughing ones.—M. C. Lang, *per Med. Annu.*, 1931, 278.

**PLEURITIC EFFUSION.** Iodoform intrapleurally, as an emulsion in glycerin, olive oil and ether (1 in 9), in 1 or 2 doses of 1 to 2 ml., gave good results.—*Per Practitioner*, i/1928, 264.

**Carbasus Iodoformi (B.P.C.).** IODOFORM GAUZE. 5%.

**Glycerinum Iodoformi (B.P.C.).** *Syn.* EMULSIO IODOFORMI.

Iodoform, in fine powder, 1, alcohol 90% *q.s.* to moisten, glycerin 7, sterilised water 2. Mix well in above order. *K.C.H.* has iodoform (washed with 1 in 20 phenol solution) 1 part, glycerin 9 parts.

For injection, well diluted, into the bladder and into sinuses. Most effective before caseation has occurred. For filling a cavity in the bone, after removing caseating tissue, iodoform 1 and boric acid 4 is useful.

**Guttæ Iodoformi Compositæ (Brompton H.).** (For the ear).

Iodoform 5 gr., ethyl acetate 2 dr., alcohol 90% 2 dr., glycerin to 1½ oz.

**Injectio Iodoformi.** (For bladder injection.)

Iodoform in fine powder 1, mucilage of tragacanth 2, water 7. This is less irritating than the glycerin emulsion (should be diluted 20 to 40 times with warm water).

**Insufflatio Iodoformi.**

Iodoform 2, starch (carefully dried) 1. In specific affections of the throat, antiseptic and mildly caustic.

**Oculentum Iodoformi (B.P.).** 4% in Oculentum Simplex.

[P2] **Pasta Iodoformi (R.D.H.).**

Iodoform 6, tannic acid 1, liquefied phenol *q.s.* to make a paste.

**Cinnamon Paste (Iodoform Paste)** is used by dentists and understood to mean iodoform mixed into a paste with cinnamon oil. Used for treating septic root canals.

**Pasta Zinci et Iodoformi.** *Syn.* Z.I.P.P.

Zinc oxide 1 oz., iodoform 1 oz., liquid paraffin 10 fl. dr.

A modification of bismuth and iodoform paste (*see* p. 314), which is said to be safer and more effective since there is less risk of iodoform poisoning accompanying its use. It is used in the treatment of wounds, ulcers, etc.

**ULCERS.** All forms of chronic ulcers except those with a circular outline and clean-cut edges heal rapidly when treated with "Zipp." The "Zipp" is spread thickly on three or four thicknesses of gauze cut to a size to cover the whole ulcerated surface, pressed evenly on to the part affected, covered with a bandage made of several thicknesses of gauze bound evenly and firmly over it, and a plaster of Paris bandage then applied. The dressing should be left for three weeks or longer, by which time the ulcer may be found healed. If there is sloughing the bandage may need taking down and a new one applying after a week, at all events as soon as any discharge appears on the surface of the plaster, or tracks down below the lower end of the plaster.—W. C. Dale, *West African Med. J.*, Nov. 1935, 16, per *Trop. Dis. Bull.*, 1936, 630.

It may be used as a routine in the treatment of chronic ulcers and in the post-operative treatment of acute osteomyelitis, the affected limb being afterwards encased for at least a week in plaster of Paris. The paste also has a remarkable deodorant action on offensive discharge.—W. K. Connell, *Brit. med. J.*, i/1940, 273.

**Pigmentum Iodoformi Compositum (B.P.C.).** *Syn.* IODOFORM VARNISH, WHITEHEAD'S VARNISH.

10% w/v with benzoin, storax and balsam of tolu in ether. For surgical use.

**Pigmentum Iodoformi (Gt. Orm. H.).** WHITEHEAD'S VARNISH MODIFIED. Iodoform 1 dr., benzoin varnish 10 dr. (Benzoin varnish is: Benzoin 4 dr., colophony 3 dr., balsam of tolu 1 dr., ether (0.720) 5 oz.).

Cheap and effective: does not retract the skin, dries well, and remains elastic. Clean, antiseptic, and mildly stimulating.—J. W. Peck, *Brit. med. J.*, ii/1931, 681.

**Pulvis Iodoformi et Acidi Borici (B.P.C.).** Iodoform 1, boric acid 3.

**Suppositorium Iodoformi (B.P.)** contains 3 gr. of iodoform in oil of theobroma. 1 gr. and 5 gr. suppositories are also made. For fissure of the anus and irritating hæmorrhoids.

**Unguentum Iodoformi (B.P.C.).** 10% in simple ointment. *R.L.O.H.* has 60 gr. in yellow soft paraffin to 1 oz. *Fr. Cx.* has 10% in soft paraffin.

[P1-S1] **Unguentum Iodoformi cum Atropina (R.L.O.H.).**

Iodoform 1 dr., atropine 2 gr., yellow soft paraffin to 1 oz. Heat the yellow soft paraffin to 61°, add the atropine dissolved in sufficient chloroform to make a saturated solution, and finally add the iodoform. Stir till cold.

**Unguentum Iodoformi et Eucalypti (B.P.C.).** Iodoform 2% and oil of eucalyptus 20% in a paraffin basis.

**Mencièr's Solution "A."** As a wound dressing. Iodoform 10, Peruvian balsam 30, guaiacol 10, eucalyptol 10, ether 100.

**Solution "B"** is the same with ether to 1000.

**Æthyleni Periodidum (Fr. Cx.).** *Syn.* DI-iodoform, ETHYLENE TETRAIODIDE.  $C_2I_4 = 531.7$ .

Yellow crystalline substance, odourless and containing about 95.5% of I. Insoluble in water, alcohol and ether; soluble in chloroform, benzene and carbon disulphide. It decomposes in light and is used as a substitute for iodoform. *M.p.* 192°.

## IODUM

*B.P.*, *U.S.P.* XI, *Fr. Cx.*, *P. Jap. V*, *P. Helv. V*, *P. Dan.*

*I* = 126.9.

**Dose.**—*U.S.P.* average dose  $\frac{1}{2}$  grain. *Fr. Cx.* has max. single dose 0.02 g.; max. in 24 hours 0.2 g.

In heavy, bluish-black crystals or plates. Is obtained from kelp or from the mother liquors of Chili saltpetre.

The following medicinal inorganic iodides contain the halogen approximately in these proportions:—Ammonium iodide 87.5%, lithium iodide, 94.75%, potassium iodide 76.4%, sodium iodide 84.6%, strontium iodide ( $\text{SrI}_2 \cdot 6\text{H}_2\text{O}$ ) 56.45%.

**Soluble.** About 1 in 5000 of water, 1 in 12 of alcohol 90%, 1 in 4 of ether, 1 in 30 of chloroform, 1 in 65 of glycerin, 1 in 6 of carbon disulphide and 1 in 9 of benzene. Very soluble in concentrated solutions of potassium iodide.

**Incompatible** with alkalis, alkaloids, starch, soluble lead and mercury salts, phenol, chloral hydrate and sodium thiosulphate.

**Antidotes.** Give copious draughts of mucilage of starch, or flour, etc., and water; or 20 to 30 gr. of sodium thiosulphate in water. Then empty stomach by emetic or by stomach tube, using thin starch or dilute sodium thiosulphate solution. Keep the patient warm; give demulcent drinks freely. Strychnine,  $\frac{1}{4}$  gr., hypodermically. Morphine,  $\frac{1}{4}$  gr. hypodermically, if pain is severe.

The fatal dose is usually about 2 or 3 g., but recovery is said to have occurred after 10 g. The prognosis is generally favourable.

During a 21-year period (1915 to 1936) 27% of all the patients admitted to the Boston City Hospital after suicidal attempts had ingested iodine, usually in the form of tincture. The number of these cases was 327 out of 1195 attempted suicides. Not one death due to iodine poisoning occurred among these patients. Between 1931 and 1937 there were 18 successful suicides by iodine in New York City, the dose ingested varying between 1 and 8 ounces. Death in all cases occurred within 48 hours.—M. Moore, *New Engl. J. Med.*, 1938, 219, 383.

**Iodine burns** may be successfully treated by the use of dressings soaked in a 1 in 200 aqueous solution of sodium thiosulphate. This solution will also quickly remove iodine stains from the skin.—H. P. Towle and J. L. Grund, *New Engl. J. Med.*, ii/1937, 475.

**IODIDE ERUPTION**, a case of granulomatous form which is rare. Treatment was sodium chloride 10 to 20 gr. three times daily after meals. Said to have been attended with dramatic effect in cases of bromide eruption. Slow recovery.—H. C. Semon, *Lancet*, ii/1926, 803.

Fatal dermatitis following iodine spirit ( $2\frac{1}{2}\%$  in industrial methylated spirit) for operation; sodium thiosulphate used to counteract. Pronounced idiosyncrasy no doubt.—R. C. Alexander, *Brit. med. J.*, ii/1930, 101.

Further cases.—D. G. De Bouk, *Brit. med. J.*, ii/1930, 162. A man applied Tinct. Iodi Mit. to the arm for rheumatism. Caused a mass of blisters from head to foot. In bed 6 weeks.—L. Schapera, *ibid.*, 194.

Free application to the arms caused dermatitis. Vesicles turning to pustules. Temperature  $103^\circ\text{F}$ . Starch poultices used, also sodium bicarbonate, subsequently Lin. Calcis. Alcoholic iodine solutions are in their nature irritants. Their application to areas already denuded of surface protection open to risk.—O. Thomas Jones, *Brit. med. J.*, i/1931, 15.

**Uses.** Iodine is an antiseptic and irritant. *Internally*, small doses cause mild irritation of the mucosa of the stomach and improve appetite, but more frequently they give rise to nausea, discomfort, and vomiting, and repeated small doses may result in iodism, namely, nasal catarrh, gastric upset, and lachrymation. Iodine is absorbed in the form of iodides and its fate in the body is precisely similar to that of iodides which have replaced it for most therapeutic purposes for internal use.

The most important use of iodine is in the treatment of thyroid disease, and in particular in Graves' disease, where it is used as a pre-operative procedure to produce a rapid remission of symptoms in order to lessen the risk of thyroidectomy. For this purpose 5 m. of Lugol's solution is administered three times daily in milk. There is usually a striking improvement in the patient's symptoms within three days from the commencement of this treatment. The beneficial effects usually reach their maximum within 10 days to 3 weeks, and operation is best done during this period, the administration of iodine being continued for a few weeks subsequently. The medical treatment may actually be found sufficient of itself to clear up mild cases, especially the mild hyperthyroidism associated with a puberty goitre or post-operative hyperthyroidism.

Iodine has been used in the past in a variety of chronic conditions such as syphilis and tuberculous disease of the bones and glands, and of other organs, but has now been almost entirely superseded by iodides.

Doses of 1 or 2 m. of the weak solution in  $\frac{1}{2}$  ounce of water every half hour are stated to be beneficial in cases of vomiting, and good results are claimed from the use of the tincture in a dose of 5 drops twice daily (2 drops for children) in the treatment of acute diarrhoea or chronic colitis.

*Externally*, iodine acts as an irritant. Applied to the intact skin it exerts a mild lasting irritation which induces some congestion of the subcutaneous tissues, and it is employed in the form of tincture or ointment in the treatment of numerous chronic inflammatory conditions such as pleurisy, phlebitis, periostitis, arthritis, enlarged cervical glands and orchitis (after the acute inflammation has subsided). Blepharitis is also benefited from the application of the weak tincture to the lid margins after removal of crusts, and corneal ulcers, especially the herpetic forms, may with advantage be touched with the tincture after cocaineization. Applied in concentrated solution to the skin it may cause blistering and vesication.

Iodine has a powerful germicidal action and is used for disinfecting the skin prior to operation. It is generally employed in a strength of  $2\frac{1}{2}$  to 5% in 10% potassium iodide solution or in alcohol, and is painted on the site of operation a few minutes before an incision is made. Unfortunately, its bactericidal action is much reduced by proteins, and in the treatment of open and infected wounds it has now been largely replaced by acriflavine. It is of interest to note that iodine is no longer used for wound antisepsis in the Army Medical Services.

The application of a  $2\frac{1}{2}$  to 5% alcoholic solution has also been found of value in infections of the cervix uteri, vagina and vulva, and a  $1\frac{1}{2}$ % solution with potassium iodide in glycerin (Mandl's paint) is a useful application in tonsillitis.

Iodine also possesses a marked parasiticial action and a 1 to 5% tincture is of value in ringworm of the scalp or body and in mycotic affections such as athlete's foot, dhobie's itch, etc.

Although it has been used in various forms and by various routes, the *parenteral administration* of iodine has not met with any great measure of success apart from its employment in the form of iodised oil in the X-ray diagnosis of bronchiectasis. Hydrocele has been treated by the injection of tincture of iodine or Lugol's solution into the sac after aspiration, but the treatment is extremely painful and the end-result uncertain. Intravenous injections have been employed in numerous acute conditions such as pneumonia, plague, septicæmia, etc., but their value is doubtful and their use not without risk.

For *inhalation* a few drops of the weak solution are added to hot water, often with the addition of creosote or phenol, and the vapour inhaled in phthisis or chronic bronchitis.

Various articles containing small proportions of free or combined iodine such as locketts, soap and socks have been marketed, but their therapeutic effect is very doubtful and their action probably purely psychological.

#### REFERENCES TO IODINE THERAPY

**ACTINOMYCOSIS.** Tincture of iodine in milk. *Dose*.—5 to 10 minims in half a cup of water three times a day. "Effect almost incredible."—H. Chitty, *Brit. med. J.*, i/1926, 419; i/1929, 347. See also *Prescriber*, 1929, 345.

**CORNEAL ULCERS** treated by a 1:20 or 1:30 tincture of iodine after preliminary use of cocaine. The iodine is taken up on a probe or glass rod and held in the air a minute or two for the alcohol to evaporate, then the ulcer touched with it. The iodine is therefore almost solid and cannot diffuse. See also Eye affections, under Intravenous Iodine *postea*.

**TONSILS.** Diseases of, due to fungi, well treated by application of dilute tincture of iodine and large doses of potassium iodide—as much as 30 gr. thrice daily.—Sir A. Castellani, *Prescriber*, 1930, 67.

**TUBERCULOUS ULCERS** and others treated by sodium iodide internally, 15 gr. three times a day with hydrogen peroxide and a little acetic acid locally on cotton wool.—S. A. Pfannenstill, *Brit. med. J.*, i/1925, 732.

The administration of minute amounts of iodine ( $\frac{1}{16}$  or  $\frac{1}{8}$  gr. every 5 days in butter-scotch) was found to give great improvement in pre-tubercular children when cod-liver oil, etc., had failed. Chronic bronchitis and allied conditions also respond well.—K. Fraser, Cumberland, School M.O. Report, 1925.

**VARICOSE ULCERS.** In most patients the best of all local dressings for leg ulcer is starch iodide paste which, combined with sufficient rest in bed, controls pain after 24 hours' use, allows of discharge in three days or so, and will heal even multiple extensive ulcerations of the leg of so hopeless an aspect as almost to compel amputation. The best formula for the paste is: Starch 1 oz., glycerin 2 oz., distilled water 6 oz. Boil together and when nearly cold stir in  $\frac{1}{2}$  oz. of strong solution of iodine (*B.P.* 1885). The result is a non-greasy homogeneous paste, clean in use, which is spread half an inch thick on to the smooth surface of lint and applied, then covered with wool and a very firm bandage.—S.W. Smith, *Brit. med. J.*, i/1940, 147.

**VARICOSE VEINS** have been treated by injecting 1% solution of iodine made with potassium iodide (Schiassi's method).

**WHITLOW** may be successfully treated by the application of iodine to the gaping junction of the skin and nail-plate in the neighbourhood of the lunula; it is essential that the iodine should run completely round the nail, and if this does not occur spontaneously the skin above the lunula should be slightly raised. The treatment should be carried out twice daily and also when the hands are washed.—W. G. Harvey, per *Practitioner*, ii/1939, 122.

#### Intravenous Iodine Injection.

**EYE AFFECTIONS.** For papillitis, retinitis pigmentosa, optic atrophy, or optic neuritis, treat root cause. Give iodine intravenously: ( $\frac{1}{2}$  gr. each of iodine and

potassium iodide in 10 ml. of distilled water) every 3 or 4 days up to 6 injections, rub mercurial ointment into the temples daily and give deep injections of  $\frac{1}{2}$  to 1 ml. of mercuric cyanide 1 in 2000 with procaine hydrochloride. Marked progress with this treatment, a notable feature being the rapidly improved vision after iodine injections. Where there are no prominent veins, the following is given intramuscularly—Sodium iodide 250 gr., iodine 200 gr., liquefied phenol 3 dr., distilled water 4000 ml., 10 ml. injected into gluteal muscles every 6 or 8 days. The mixture should not be stirred up.—E. R. Shetti, *Brit. med. J.*, ii/1930, 1098.

**PLAGUE.** Early cases of bubonic plague well treated with iodine intravenously, 5 to 10 ml. daily for 4 days of solution of iodine 18 gr. and potassium iodide 36 gr. in normal saline 4 oz., together with a mixture containing potassium iodide and stimulants, every 4 hours. Buboec treated by  $\frac{1}{2}$  gr. of mercuric chloride in 2 ml. of water hypodermically in lymphatic area drained by groups of glands in which bubo formed.—*Indian med. Gaz.*, 1926, 63.

**PNEUMONIA AND CELLULITIS** have been treated with initial dose of weak solution 20 m. in 10 ml. of normal saline, increased by 10 or 20 m., according to reaction, up to 60 m.—A. B. de Castro, *Indian med. Gaz.*, 1925, 141, and S. N. Datta, *ibid.*, 579. See also *J. trop. Med. (Hyg.)*, 1927, 225.

Pneumonia, erysipelas, cellulitis, rheumatism, septic wounds and bad cases of phagedenic ulcers well treated. Iodine 24 gr., potassium iodide 36 gr., distilled water to 1 oz. *Dose.*—1 to 2 ml., diluted with 8 ml. distilled water and given once or twice weekly.—E. Burke, *Brit. med. J.*, ii/1927, 1062.

Collosol iodine intravenously of value in pneumonia. 10 ml. of a 0.4% solution is given every four hours from noon to midnight (i.e., four doses). A striking and constant result is the immediate fall of the temperature by lysis. Fever usually terminates before the seventh day, patients are easier to nurse, and mortality is diminished.—A. Goodall, *Edinb. med. J.*, ii/1937, 133.

**Balneum Iodi (B.P.C.).** Contains 4 oz. of strong solution of iodine per 30 gallons.

**Cataplasma Iodi (B.P.C.).** Weak solution of iodine, 2 dr., in linseed poultice.

[P1] **Chloroformum Iodi.** 1 in 30.

Stains less and does not promote desquamation, itching or dermatitis like the alcoholic solution.

**Collodium Iodi (B.P.C.).** Iodine  $6\frac{1}{2}\%$  w/v in flexible collodion.

**Glycerinum Iodi.** Iodine 1, glycerin 50. Heat carefully until dissolved. A useful pigment; the skin does not harden by repeated application, nor peel off. Water helps solution, cf. Morton's Fluid.

For internal use this preparation is quite suitable diluted with water, with which it mixes temporarily. *Dose.*—On lines of the *Tinctura Iodi Fr. Cx.* 1908 method of use. It is approximately  $\frac{1}{3}$  the strength.

[P2] **Inhalatio Iodi Composita (L.H.).** *Dose.*—10 minims on an oro-nasal mask.

Cresote 2, phenol 2, spirit of chloroform 2, weak solution of iodine 1, spirit of ether 1.

For early pulmonary tuberculosis by inhalation from a "Burney Yeo" inhaler. It must be continuous and in operation the whole of the 24 hours, excepting meal times. Six to 8 drops are used on the sponge of the inhaler every hour during the day, and two to three times during the night if awake. Non-irritating, beneficial and does not cause hæmoptysis. Allays pyrexia and cough.

**Injectio Iodi (C.L.T.H.).** *Syn.* MORTON'S FLUID. *Distinguish from the douche, which is also called "Injection."* Iodine 10 gr., potassium iodide 30 gr., water 25 m., dissolve and add glycerin to 1 oz. *Glycerin Iodi (St. T. H.)* is the same without the water.

In spina bifida 30 m. have been injected into the tumour, also into a soft solid goitre.

**Injectio Iodi (C.H.W., L.H.).** IODINE DOUCHE. Weak solution of iodine 1 dr., water 1 pint. For injection in puerperal sepsis. Gangrene of the vulva, vagina and cervix has been treated by a douche of normal saline, cutting away the gangrenous parts, then giving a weak iodine douche, followed by packing with balsam of Peru gauze.



**Injectio Iodi Fortissima.** *Dose.*—3 to 5 minims.

Iodine 360 gr., potassium iodide 360 gr., distilled water  $4\frac{1}{2}$  dr. Measures exactly 1 oz. and contains  $\frac{1}{2}$  gr. of free iodine in each minim. For fibrous bronchocele.

A grain of iodine may be held in solution in a minim of fluid, by employing sodium iodide in the proportion of iodine 3, sodium iodide 2, and water *q.s.* to 3 volumes.

**Insufflatio Iodi et Acidi Borici (Aural) (U.C.H.).** *Syn.* PULVIS ACIDI BORICI CUM IODO.

Iodine 0.75, boric acid 99.25. Dissolve the iodine in alcohol and triturate with the boric acid.

The following formula is suggested:—Iodine 2 gr., potassium iodide 1 gr., anæsthetic ether 90 m., boric acid in powder 260 gr. Dissolve the iodine and the potassium iodide in the ether in a glass mortar. Add the boric acid, previously sifted. Stir for exactly three minutes for the ether to evaporate. The presence of potassium iodide gives the powder increased stability, and the use of ether as the solvent greatly reduces the amount of iodine lost during preparation.—H. Finemore, *Aust. J. Pharm.*, 1939, 1038.

Sulzberger's formula for iodine-boracic powder for aural insufflation specifies a mixture of one part of resublimed iodine in 99 parts of boracic powder. If stored in green stoppered bottles it keeps satisfactorily for some weeks.—*Practitioner*, i/1939, 230.

**OTORRHEA, CHRONIC.** Cures nearly 95% of chronic cases. The discharge is mopped or sucked out and the powder blown through the perforation into the middle ear until the deepest part of the meatus is full. The powder readily dissolves in the discharges within 48 hours.—R. Scott Stevenson, *Brit. med. J.*, i/1933, 95.

Insufflation of boric acid with 0.75% of iodine is more satisfactory than any other method. 96 cases treated with history of 4 weeks to 25 years—all dried up with from 1 to 30 treatments.—R. H. Bettington, *Med. J. Aust.*, 1935, 747.

**Boro-Iodine** (*Duncan, Flockhart, Edinburgh*). A finely divided mixture of iodine 1% in boric acid for the treatment of chronic uncomplicated suppurative otitis media.

**Iodocholeate.** Iodine combines with bile acids to form tri-iodo derivatives which are soluble in water and in alcohol, but not in other organic solvents. Although the compounds give the starch reaction for iodine and the iodine content can be determined by direct titration with thiosulphate, aqueous solutions can be concentrated in open containers on a water-bath practically without any loss of iodine. Solutions of equivalent iodine content are more effective germicides and are less irritating than the pharmacopœial solutions.—P. Goedrich, *J. Amer. pharm. Ass.*, 1937, 509.

An aqueous solution with an addition of 15 to 20% alcohol is the most desirable form, and for therapeutic purposes a solution of 1 to 2.5% is most suitable. A 2.5% ointment may also be prepared as in the following formula:—Iodocholeate powder 11.7 g., oxycholesterol-petrolatum base 38.3 g., distilled water 10 ml. Because the iodine in iodocholeate is adsorbed to the bile salt it is less volatile and combines less readily with protein. Thus, compared with tincture of iodine, it is less irritating, has greater fungicidal power in the presence of protein, and is active over a longer period. Either in solution or ointment it has proved valuable in the treatment of fungous infections of the skin.—W. F. Lever, *Arch. Derm. Syph.*, ii/1939, 19.

**Liquor Iodi Æthereus (B.P.C.).** *Syn.* TINCTURA IODI ÆTHÆREA.  $2\frac{1}{2}\%$  *w/v* in ether.

**Liquor Iodi Aquosus (B.P. Add. I).** *Syn.* LUGOL'S SOLUTION (*Fr. Cx.*), LIQUOR IODI COMPOSITUS.

*Dose.*—5 to 15 minims (0.3 to 1 ml.).

Iodine 5% *w/v* and potassium iodide 10% *w/v* in water. 15 m. contains about  $\frac{1}{2}$  gr. of free I and about 2 gr. of total I.

B.P.C. is similar but has 5% *w/v* of each. U.S.P. XI is same as B.P. Add. I with wider limits. *Average dose.*—3 minims.

**Liquor Iodi Decoloratus (B.P.C.).** *Syn.* TINCTURA IODI DECOLORATA.

This solution contains ammonium iodide and ammonium iodate equivalent to about 3% *w/v* of iodine. A useful application for chilblains and for painting on exposed affected parts.

**Liquor Iodi Decoloratus Fortis** (*syn.* TINCTURA IODI DECOLORATA FORTIS) is occasionally ordered. It is prepared by dissolving iodine 2.85 g. in alcohol (90%) 27.5 ml., adding strong solution of ammonia 6.25 ml., and keeping in a warm place until decolorised.

**Liquor Iodi Fortis (B.P.).** *Syn.* TINCTURA IODI FORTIS, STRONG TINCTURE OF IODINE, PIGMENTUM IODI, LINIMENTUM IODI.

Contains 10% *w/v* of iodine and 6% *w/v* of potassium iodide in distilled water and alcohol 90%. Conforms with *I.A.*

**Churchill's Tincture of Iodine.** Iodine 1200 gr. and potassium iodide  $\frac{1}{2}$  oz. dissolved in water 4 oz. and diluted with alcohol (90%) to 16 oz.

**Liquor Iodi Mitis (B.P.).** *Syn.* TINCTURA IODI MITIS, TINCTURA IODI, TINCTURE OF IODINE.

*Dose.*—5 to 30 minims (0.3 to 2 ml.).

Iodine 2½% *w/v*, and potassium iodide 1.5% *w/v*, in water and alcohol 90%. The proportion of potassium iodide is not sufficient to keep the iodine in solution when diluted with water; this can be overcome by increasing the proportion from 1.5 to 2.5%.

**Tinctura Iodi Mitis (U.S.P. XI).**

Iodine 2 and sodium iodide 2.3 in sufficient diluted alcohol (48.4 to 49.5% *v/v*) to make 100.

**Liquor Iodi Oleosus (B.P.C.).** *Syn.* TINCTURA IODI OLEOSA.

Iodine 8% *w/v* and castor oil 16½% *v/v* in alcohol 90%.

Repeatedly applied does not crack the skin as the tincture does.

**Ethidol** (*Burroughs Wellcome, London*). Ethyl iodoricinoleate, a stainless non-irritating compound containing 20% of I. It may be heated to 150° for sterilisation. Used by inunction or spread on dressing in all cases in which the application of iodine is indicated.

**Liquor Iodi Simplex (B.P.).**

*Dose.*—3 to 15 minims (0.2 to 1 ml.); 15 m. contains about 1½ gr. of iodine. The dose may be gradually increased up to 25 or 30 m. thrice daily.

Iodine 9% *w/v*, in alcohol 95%. This corresponds to approximately 10% *w/w* and it is therefore the same strength as **Teinture d'Iode** (*Fr. Cx.* 1908) (also *P. Hung.*), sometimes called French tincture of iodine.

It is unfortunate, since the use of this preparation is in considerable vogue, that the above tincture of *Fr. Cx.* 1908 is superseded by **Teinture d'Iode** (*Fr. Cx.* 1937). This latter preparation which is therefore now the official French tincture of iodine, contains iodine 10 g., potassium iodide 4 g., alcohol 90% 126 g., and water 10 g., but it is *not* the preparation usually required when French tincture is asked for in this country. Unless otherwise directed **Liquor Iodi Simplex (B.P.)**, equivalent in strength to the original tincture of *Fr. Cx.* 1908, should be dispensed for "French Tincture of Iodine."

Loss of free iodine is rapid during the first two months after manufacture but equilibrium is reached in about eight months with a total loss of about 20% of free iodine.

The "intensive iodine treatment" of tuberculosis was advised by L. Bourdreau. The treatment is also of value in arthritic cases, chronic gout and "rheumatic gout." *As much as 10 grains of iodine per diem can be given.* There may be slight catarrh of the nasal mucous membrane, but no iodism as from potassium iodide. The iodine is probably deposited on the stomach lining and slowly absorbed. The patient places the dose (15 drops equal approx. 10 minims) in a glass and adds half a tumbler of water. It may also be given in milk or as a mixture of equal volumes of simple tincture of iodine, spirit of chloroform and glycerin which form a clear solution containing 1 gr. of iodine in about 30 m.

**Nebula Iodi Composita (B.P.C.).** Iodine 1% *w/v* and phenol  $\frac{1}{2}$ % *w/v* in light liquid paraffin.

**Nebula Iodi et Mentholis (B.P.C.).** Iodine 2% *w/v* and menthol 4% *w/v* in light liquid paraffin.

**Neb. Iodi c. Phenol. (N.I.F.).**

Iodine 2 gr., phenol 8 gr., menthol 5 gr., camphor 2 gr., light liquid paraffin to 1 oz.

**Parogenum Iodi (B.P.C.).** *Syn.* IODINE VASOLIMENT, LINIMENTUM IODI PETROLATUM. 10% *w/v*.

**Vasogen Iodine (Pearson, Mitcham)** (previously marketed as IODINOSOL). Preparations containing 6% or 10% of iodine in a partly oxygenated mineral oil for use by inunction. Also available in capsules containing 10 m. of the 6% preparation.

**Pigmentum Iodi Compositum (B.P.C.).** *Syn.* PIGMENTUM MANDL, MANDL'S PAINT.

Iodine  $1\frac{1}{2}$ % *w/v*, with potassium iodide and oil of peppermint, in a glycerin medium. It should be well shaken before use since the oil of peppermint is insoluble and rises to the surface on long standing. Used as a throat stimulant and in tonsillitis.

**Pigmentum Iodi et Ætheris Acetici (J. Dundas Grant).**

Equal parts of simple solution of iodine, ethyl acetate and glycerin. This mixes quite well and is not unpleasant.

**Pigmentum Iodi cum Formaldehydo (M.H.).**

Solution of formaldehyde 10 m., weak solution of iodine 1 dr., oil of peppermint 2 m., glycerin to 1 oz. For granular pharyngitis.

**Pigment. Iod. Fortis. (N.I.F.).**

Iodine 44 gr., potassium iodide 27 gr., boric acid 9 gr., distilled water 48 m., industrial methylated spirit without acetone to 1 oz. It contains about 10% of I.

**Pigment. Iod. Mit. (N.I.F.).**

Strong iodine paint (N.I.F.) 120 m., boric acid 7 gr., industrial methylated spirit without acetone to 1 oz. It contains about 2.5% of I.

**Pigment. Iod. (N.I.F.).**

Strong iodine paint (N.I.F.) 4 dr., boric acid 5 gr., industrial methylated spirit without acetone to 1 oz. It contains about 5% *w/v* of iodine.

**Pigmentum Olei Picis cum Iodo (B.P.C.).** *Syn.* PASTA IODI ET PICIS, COSTER'S PASTE.

Iodine 1 by weight dissolved with the aid of gentle heat in rectified oil of tar 4 by volume.

**Uses.** For ringworm of the scalp; after well shaking the bottle the paint is well brushed in with a stiff brush. A scab will be produced which should be removed in a few days, the part cleansed by soaking with oil, and then soap and warm water; after drying, more paste should be applied. It seldom causes pain.

**Syrupus Iodotannicus (B.P.C.).**

**Dose.**— $\frac{1}{4}$  to 1 drachm (1 to 4 ml.).

Iodine and tannic acid, 1% *w/w* of each, in syrup and syrup of lemon.

The *Fr. Cx.*, *P. Ital. V*, *F.E. VIII*, *P. Belg. IV*, and *P. Ned. V* syrup is only  $\frac{1}{2}$  this strength, *viz.* 0.2% of iodine.

**Uses.** Of value for enlarged glands in children and also as a tonic after removal of tonsils and adenoids.

Specially useful in cases of chronic lymphadenitis associated with or independent of adenoids. In atrophic rhinitis has given good results especially when combined with arsenic, also in simple bronchocele. In arteriosclerosis it is often more valuable than iodides.

**Syrupus Iodotannicus cum Phosphate (B.P.C.).**

*Dose.*— $\frac{1}{2}$  to 1 drachm (1 to 4 ml.).

Contains about  $2\frac{1}{2}$  gr. of calcium phosphate per dr. of iodotannic syrup. *Fr. Cx.* has 2% of calcium phosphate.

**Unguentum Iodi (B.P.C.).**

Iodine 4% with potassium iodide, in a simple ointment basis.

**Unguentum Iodi (U.S.P. XI).** Iodine 4, potassium iodide 4, glycerin 12, wool fat 5, yellow wax 5, petrolatum 70. It must contain from 6.5 to 7.5% of total iodine.

**Unguentum Iodi Denigrescens (B.P.C.).** *Syn.* NON-STAINING IODINE OINTMENT. Contains iodine in arachis oil and soft paraffin.

For use in rheumatic affections, enlarged glands, and sprains.

Non-staining iodine ointment shows large variations in iodine content due often to the method of preparation. Alternative methods are proposed and it is pointed out that in all methods of preparation subsequent heating after the incorporation of the iodised oil with the soft paraffin will yield a deposit of resin-like substance.—J. C. Penman, *Quart. J. Pharm.*, 1939, 380.

**Unguentum Iodi Intinctum.**

Iodine 1, oleic acid 4; heat to effect absorption and mix with yellow soft paraffin 14 and hard paraffin 1 previously melted together.

**Iodex (Menley & James, London).** A stainless iodine ointment containing 4% of iodine. Also made with methyl salicylate 5%. Suppositories are made equivalent to  $\frac{1}{2}$  gr. of iodine in a neutral base.

**Iodermiol (Hewlett, London).** An ointment containing about 5% of iodine which does not harden or discolour the skin. Also made with methyl salicylate.

[P2] **Vapor Iodi Æthereus (B.P.C.).** Ethereal solution of iodine 25% *v/v*, phenol 25% *w/v*, creosote 12.5% in alcohol 90%. 10 m. to be used in an inhaler.

**Oleum Iodisatum (B.P. Add. I).** *Syn. and Prop. Names.* OLEUM IODATUM (*U.S.P. XI*), IODATOL (*British Drug Houses, London*), IODINOL (*Martindale, London*), IODIPIN (*Merck, Darmstadt; Martindale, London*), LIPIODOL (*Guerbert, Paris; Bengué, London*), NEO-HYDRIOL (*Pharmaceutical Specialities (May & Baker) Ltd., London*), OLIOLASE (*Corbière, Paris; Anglo-French Drug Co., London*).

Iodised oil is an iodine-addition product of poppy-seed oil and may be prepared by treating poppy-seed oil with hydriodic acid. It is a colourless or pale yellow viscous oil with slightly alliaceous odour and contains 39 to 41% of combined iodine.

Weaker preparations, containing 10% or 25% of iodine, are also available under the above proprietary names. They are usually preferred to the 40% oil for internal administration, and can also be given hypodermically.

Iodised oils are prepared by saturating fatty oils containing unsaturated fatty acids with reagents such as iodine monochloride. One method consists of treating iodine trichloride 75 g., with 200 ml. of cold water until a clear orange solution is obtained. The resultant mixture, which contains iodine monochloride, is cooled in ice and 100 ml. of sesame oil previously cooled to 0° is added in small quantities with constant shaking during the course of 15 minutes. The mixture is vigorously shaken until a thick white emulsion is obtained. The emulsion is allowed to stand in the dark for one hour, transferred to a separating funnel with the aid of 100 ml. of chloroform, shaken, and allowed to stand in the dark to separate. The organic solution is run off, washed with water and dried over calcium chloride. The solvent is removed and the residual liquid cooled.—S. Rangaswami, *Indian J. Pharm.*, 1940, 2, 3.

**Contraindications.** High fever, marked intolerance to iodine, grave septic conditions of the lung and active tuberculosis.

**Uses.** Iodised oils containing 40% of iodine are employed to render the bronchi and their ramifications opaque to X-rays, their chief value lying in their ability to show the presence or absence of non-obstructive bronchiectasis, and when present, even in the early stages, its locality, extent and type. They are non-irritant to the mucous membrane, etc. After injection in the bronchi they are absorbed in the lung, and iodine can be detected in the urine for many days after; hence, they are antiseptic agents rational in the treatment of chronic affections of the lower respiratory tract. There are various methods of administration of the oil, the simplest being by the mouth. The patient should be seated with his head on his hand and his elbow on a rest, the operator in front. The tongue is protruded and a blunt-ended cannula placed over its base between the pillar of the fauces and the uvula. The warm oil (100°F.) is given with a 20 ml. syringe, while the patient breathes slowly and regularly. If the patient heaves it is useless to continue. He should lean to the side injected and be semi-recumbent with head lowered. This method is unsuitable, however, for children and nervous patients, to whom the oil is administered by injection into the trachea through the crico-thyroid membrane (for further details of this and other methods see Vol. II, 21st Edn.). In all cases the patient should first be tested for iodine intolerance with potassium iodide. The amount of iodised oil used varies from 5 ml. to 40 ml., the average being 20 ml. For outlining the bronchial tree from 6 to 10 ml. is sufficient.

The possible dangers from the use of the procedure are symptoms of iodine poisoning (this only applies with the crico-thyroid route), injury to local tissues in the neck, and bronchopneumonia resulting from dissemination of infection throughout the lung. Minor symptoms, which normally disappear in 24 hours, are injection malaise, anorexia, and headache. In pulmonary tuberculosis the injections are undesirable, and its use is dangerous in patients with advanced bronchiectasis with foul secretion.

The resulting pictures are excellent and there is no irritation of the mucous membrane.—F. G. Chandler, *Brit. med. J.*, ii/1928, 1157.

The injection of iodised oils is essentially a surgical procedure, introducing a foreign and possibly irritant body and involving more or less risk, which should be weighed against the presumptive advantages in comparison with the relative advantages and disadvantages of other measures. Cautions which should be especially borne in mind are (1) aged and darkened oils should never be used.

(2) Subarachnoid injections should only be used when all other means of diagnosis have been exhausted. (3) Intratracheal and intrapleural injections should be avoided in tuberculosis of the respiratory organs. (4) Injection pressure should be carefully controlled so as not to lacerate tissues. (5) Intradermal injections should only be made under fluoroscopic examination. (6) Iodised oil should not be used for renal pyelography except as an emulsion, and injections stopped if pain is felt. (7) Intravascular injections appear too dangerous.—Council on Pharmacy and Chemistry, A.M.A., *J. Amer. med. Ass.*, ii/1932, 1946.

**X-RAY PICTURES OF THE MALE URETHRA.** Shadows obtained with Iodinol 40% very satisfactory. No irritation of the urethral mucous membrane. A urethral pouch demonstrated at the Midland Medical Society.—G. P. B. Huddy, June 6th, 1929.

For giving shadows of the uterus and fallopian tubes found satisfactory at Cardiff Royal Infirmary. No toxic symptoms.—W. Panes, June 20th, 1929.

**Diodone.** *Syn. and Prop. Names.* DIODRAST, PER-ABRODIL (*Bayer Products, London*), PYELOSIL (*Glaxo Laboratories, London*).

*Dose.*—20 ml. of a 35% *w/v* solution; for children 8 to 10 ml., and for infants 2 to 3 ml.

A mixture or a loose combination of 3, 5-diiodo-4-pyridone-N-acetic acid,  $C_5H_4ONi_2 \cdot CH_2 \cdot COOH$ , and diethanolamine. It is a clear, almost colourless liquid containing 49.8% of iodine.

**Contraindications.** Nephritis, renal and hepatic insufficiency, tuberculosis and other forms of grave general illness.

**Uses.** Diodone is used as a contrast agent for excretion pyelography, and also for the contrast radiography of arteries, veins, joints and the biliary tract. The patient should be given an aperient on the night preceding the examination and on the day of the examination food should be withheld. In addition, fluid intake should be restricted for several hours before injection to increase the concentration of the diodone. Prior to injection the solution should be warmed to about 37°, and then injected through a moderately fine needle, the time of injection being about 1 to 3 minutes.

**Iodoxylum** (*B.P. Add. III*).  $C_8H_5O_5Ni_2Na_2 = 493.0$ . *Syn. and Prop. Names.* NEO-IOPAX (*N.N.R.*), PYELECTAN (*Glaxo Laboratories, London*), PYLUMBRIN (*Boots, Nottingham*), UROPAC (*Pharmaceutical Specialities (May & Baker) Ltd., London*), URO-SELECTAN B (*Schering, London*).

*Dose.*—150 to 225 grains (10 to 15 g.), usually given as a 75% aqueous solution. For children the dose is reduced proportionate to age.

The disodium salt of N-methyl-3 : 5-diiodo-4-pyridone-2 : 6-dicarboxylic acid, a white, crystalline, odourless powder containing about 51.5% of iodine.

**Soluble** 1 in 1.2 of water, 1 in 100 of alcohol 90%, but insoluble in other organic solvents.

**Contraindications.** Acute nephritis, severe renal and hepatic insufficiency, and where the urinary disease is accompanied by severe general disease.

**Uses.** Iodoxyl is used as a contrast medium for intravenous pyelography. Before use the solution should be warmed to about

blood temperature and then injected slowly through a moderately thin needle. The time of injection should not be less than five minutes. The patient should be prepared by the administration of an aperient on the day previous to the examination, and on the day itself should have no food. Further, the fluid intake should be greatly reduced for three hours before injection to increase the concentration of the iodoxy in the urinary tract. Weaker solutions are also employed for retrograde pyelography.

For anatomical information only, a single pyelogram 20 to 30 minutes after the injection suffices, but for urological purposes exposures are made at 10, 30, and 50 minutes. Before the second and third exposure the bladder should be emptied. When renal function is normal the best films are often obtained in 2 to 5 minutes after injection; with function abnormal the best results may not be obtained for 6 to 24 hours, and if function is completely suspended it is impossible to obtain a pyelogram.

The indications for intravenous urography in children are much the same as for adults. For children of 5 to 7 years give one-third the adult dose, with a reduction for younger children, but never less than a quarter of the adult dose. First film taken within 10 minutes and further films at 30 and 50 minutes after injection. To prevent gas collection in the alimentary tract (common in children) give Pulv. Glycyrrhizae Co. 48 hours before injection, and, if possible, have child up and about. With the Lysholm Fixed Bucky grid, exposures can be made in a fraction of a second. No untoward reactions. For the first time a practical routine method is provided for visualising the upper urinary tract in children.—C. G. Teall, *Brit. med.-J.*, ii/1932, 788.

**Sodium Ortho-iodohippurate.** *Prop. Name.* IODO-RAY (Martindale, *London*) (Known in U.S.A. as HIPPIURAN).  
 $C_9H_9I \cdot CONH \cdot CH_2COONa \cdot 2H_2O = 363.0$ .

A white crystalline powder containing approximately 35% of I. Soluble readily in water and alcohol.

**Contraindications.** Hepatic disease, nephritis, uræmia, and iodine idiosyncrasy. It should not be administered orally to patients with any gastric lesion.

**Uses.** Is used for intravenous, retrograde or oral pyelography. For intravenous use it is administered as a 50 to 60% solution in doses of 24 ml. for adults. For retrograde pyelography it is used in 15 to 30% solution. It may also be given orally in aqueous solution in doses of 180 grains (12 g.). Oral administration is usually less satisfactory except for children and when cystograms only are required. Following intravenous use, radiograms may be taken after about 10, 15 and 20 minutes. After oral administration pictures are usually taken in 1, 1½, 2 and 2½ hours.

Suppression of urine of a severe and alarming degree may follow the injection of the usual innocuous pyelographic mediums (Diodrast, Skiodan and Hippuran) when these are used in an amount too large to be passed successfully through a normal single kidney (four cases recorded). It seems wise in cases of unilateral or bilateral reduction of normal renal function to repeat pyelographic studies, especially by both the excretory and retrograde methods, only after a 48-hour interval.—W. C. Quinby and G. Austen, *New Engl. J. Med.*, ii/1939, 814.

**Abrodil** (Bayer Products, London) (SKIODAN in U.S.A.). Monoiodomethanesulphonate containing 52% of I and supplied in 40% solution. For excretion pyelography, dose—40 ml. of 40% solution by intravenous injection, and for retrograde pyelography, dose—10 to 20 ml. of 20% solution, instilled by means of a catheter.

**Tenebryl** (Bengué, London) is sodium diiodomethanesulphonate for intravenous urography. Dose.—15 g. in 75 ml. of water.

For further details concerning the use of contrast media see *X-ray Diagnosis*, Vol. II.

## IODINE COMPOUNDS FOR INTERNAL USE

The following preparations containing organic compounds of iodine are given internally in place of the inorganic iodides for all conditions in which the latter are indicated. The organic compounds are stated to be better tolerated and less likely to produce iodism. They are administered in syphilis, actinomycosis, goitre, arthritis, bronchial asthma, scrofula, etc.

**Calcii Iodobehenas** (*U.S.P. XI, P. Ned. V Supp. II*). ( $C_{21}H_{33}IOO$ )<sub>2</sub>Ca. *Prop. Name.* SAJODIN (*Bayer Products, London*). *Dose.*—5 to 15 grains (0.3 to 1 g.) up to 90 grains per diem after meals. *U.S.P. XI* average dose 8 grains. A tasteless powder containing not less than 23.5% of I. Insoluble in water.

**Iodo-Casein.** *Dose.*—10 to 15 grains (0.6 to 1 g.).

A yellowish brown powder containing 15% of I, used as a substitute for inorganic iodides. Insoluble in acid, and partially dissolved in alkaline solutions.

**Iodicin** (*Burroughs Wellcome, London*). A calcium salt of iodoricinoleic acid, containing 33% of I, in capsules containing the equivalent of 1 gr. of iodine (*dose.*—1 to 3, 3 or 4 times daily) and also in chocolate tablets containing the equivalent of  $\frac{1}{4}$  gr. of iodine (*dose.*—1 weekly to 1 daily) for goitre.

**Iodalbin** (*Parke, Davis, London*). An iodo-protein compound containing 21.5% of I. *Average dose.*—5 grains after meals.

**Iodamelis** (*Anglo-French Drug Co., London*). A combination of iodine and hamamelidin for use in the treatment of nutritional and circulatory affections. *Dose.*—20 to 30 drops in water twice daily.

**Iodoprotein** (*Martindale, London*). A brown powder containing about 10% of I. Also available in 5 and 10-gr. tablets. *Dose.*—10 to 15 grains (0.6 to 1 g.), or more if desired.

**Iodo-Scilline** (*Anglo-French Drug Co., London*). Iodopeptone 0.01 g., powdered squill 0.02 g., scammony resin 0.02 g. in each pill. *Dose.*—2 to 6 pills daily.

**Iodostarin** (*Roche Products, Welwyn Garden City*).

Di-iodotartaric acid,  $CH_3(CH_2)_4Cl-Cl(CH_2)_4COOH = 534.1$ , in 8-gr. tablets. It contains 47.5% of I. *Dose.*—1 to 3 tablets thrice daily. Tablets containing 5 mg. of Iodostarin are available for the prophylaxis and treatment of endemic goitre.

**Iolase** (*Anglo-French Drug Co., London*). Combination of iodine with yeast albumoses (10% I) in solution.

**Lipiodine-Ciba** (*Ciba, Horsham*). The ethyl ester of di-iodobrassicic acid, containing 41% of I. Tablets contain 0.3 g. To be taken (in place of the inorganic iodides) after the chief meals, masticating thoroughly.

**Oridine** (*Lilly, London*). Iodine in organic combination with fatty acids in chocolate tablets, each containing  $\frac{1}{4}$  gr. of iodine. *Dose.*—Prophylactic, 1 or 2 tablets until 40 are taken; treatment, 2 or 3 daily over a considerable period.

**Riodine** (*Astier, Paris; Wilcox Jozeau, London*). A 66% solution in oil of iodised glyceryl ester of ricinoleic acid (iodised castor oil), containing about 17% of iodine. Capsules contain 0.2 g. of iodised oil (=  $\frac{1}{4}$  gr. of iodine). *Dose.*—2 to 6 capsules daily. Indications as for potassium iodide; has the advantage of slow oxidation, assimilation and excretion.

**Seroden Capsules** (*Allen & Hanburys, London*). Gelatin capsules containing 1 gr. of iodine in combination with serum proteins. *Dose.*—1 to 3 capsules 2 or 3 times daily.

### Colloidal Iodine.

Colloidal iodine solution may be prepared by acting upon sodium iodide with sodium nitrite in acid dextrose solution. The nitric oxide evolved must be removed. The usual strength is 1 in 2000.

*Dose.*—1 to 4 drachms (4 to 16 ml.) *per os*. Commercial preparations are frequently solutions containing iodine in combination



with proteins. Colloidal solutions are administered in place of inorganic iodides.

**Alphidine** (*Oppenheimer, London*). Preparations of a highly assimilable, non-toxic modification of iodine for the treatment of thyroid deficiency. Tablets each contain the equivalent of  $\frac{1}{4}$  gr. of iodine. Also available as a solution (0.4% of iodine), and in combination with thyroid, etc.

**Iodeol** (*Bengué, London*). Electrically prepared colloidal solution of iodine in oil for intramuscular injection in doses of 1 ml. containing 0.2 g. of I. Used in pulmonary and rheumatic affections. Also available in capsules (= 0.25 g. of I) and suppositories.

**Iodargol** (*Bengué, London*) is a similar preparation containing 0.4 g. of I per dose, for urethral injection in infections of the urinary tract.

## IPECACUANHA

*B.P., U.S.P. XI, Fr. Cx., P. Helv. V, P. Dan., etc.*

*Syn. IPECAC.*

[P1] "*Alkaloids, the following; their salts, simple or complex:—Emetine.*"

[S1] "*Alkaloids, the following; their salts, simple or complex:—Emetine except substances containing less than 1% of emetine.*"

[S3] "*Alkaloids—Emetine—in Ipecacuanha; extracts and tinctures of ipecacuanha; substances containing less than 0.05% of emetine.*"

The dried root of *Cephaelis Ipecacuanha* (*syn. Uragoga Ipecacuanha*) (*Rubiaceæ*) from Brazil, containing not less than 2% of total alkaloids. The commonest variety is known as Rio or Matto Grosso ipecacuanha. A second variety is the Minas ipecacuanha also from Brazil. Other varieties are the Indian and Johore from the same plant, grown in Straits Settlements. They contain about 2 to 3% of total alkaloids of which about 60 to 70% is emetine.

Owing to shortage of Matto Grosso ipecacuanha, the original *B.P.* requirement that not less than two-thirds of the total alkaloids should be non-phenolic has been altered to a requirement of not less than three-fifths, the change allowing the use of varieties such as Minas and Bahia ipecacuanhas which were formerly excluded (*B.P. Add. III*).

Cartagena ipecacuanha from *Psychotria acuminata*, is not official; about 30 to 40% of the total alkaloids is emetine. It is thicker, the annulations less marked (taking the form of narrow merging ridges) and its starch-grains are somewhat larger. *U.S.P. XI* allows both *Cephaelis Ipecacuanha* (Rio) and *C. acuminata* (Cartagena) if yielding not less than 2% of ether-soluble alkaloids.

When ipecacuanha is prescribed Ipecacuanha Pulverata must be dispensed.

**Antidotes.** Emetics probably unnecessary as patient usually vomits. Give large doses of medicinal charcoal, stirred up in water. Keep patient lying down and quiet. When vomiting ceases, stimulants may be given. Morphine,  $\frac{1}{4}$  gr. hypodermically, if required.

**Uses.** In small doses ipecacuanha is an expectorant, but large doses are irritant to the gastric mucosa and produce vomiting and diarrhoea. It is employed as an expectorant in acute bronchitis when the sputum is scanty, and it gives great relief in the dry cough of laryngitis and tracheitis. It is well tolerated by children and is used in croup and whooping-cough. Combined with opium, as in Dover's Powder, it is of value as a diaphoretic in the early stages of febrile affections and especially to abort incipient colds. Although it is somewhat slow in action (taking about 20 to 30 minutes), it is probably the safest of the emetics and is valuable in broncho-pneumonia in children to empty the air-passages by vomiting. Given by the mouth, 20 gr. of powdered ipecacuanha at bedtime, in amœbic dysentery, it destroys amœbæ on the surface of the bowel wall and prevents cyst formation, but it does not affect amœbæ in the substance of the bowel wall.

To prevent vomiting after administration of ipecacuanha in the treatment of amœbic dysentery, the patient should first swallow 20 m. of Tinct. Opii (for a child  $\frac{1}{2}$  gr. of luminal is substituted for the opium), the ipecacuanha being given 30 minutes later, the patient lying on his back with the head turned to one side. Saliva is allowed to dribble out on a towel or is wiped off; it must not be swallowed and the head must not be raised. It is best given on an empty stomach the last thing at night. Another method is to mix the ipecacuanha with tannic acid in the proportion of two of ipecacuanha to one of tannic acid. This mixture (or the ipecacuanha alone) may be given in cachets or in a draught of water with mucilage. The dose of ipecacuanha is from 10 to 30 gr. once daily, and a course lasts for a fortnight. The tendency to nausea diminishes after a few days.—J. W. Barnett, *Med. Pr.*, ii/1936, 125.

An assessment of the expectorant properties of potassium iodide and ipecacuanha conducted under controlled conditions on 17 consecutive cases of chronic bronchitis, showed that the output of sputum was unchanged by the use of these drugs.—S. Alstead, *Lancet*, ii/1939, 932.

### **Acetum Ipecacuanhæ (B.P.C.).**

**Dose.**—10 to 30 minims (0.6 to 2 ml.).

Contains 5% *v/v* of liquid extract of ipecacuanha in alcohol, water and acetic acid. Alkaloidal content, 0.1%.

### **[P1-S1] Applicatio Arsenicalis Composita (Gt. Orm. H.).**

Arsenical solution 2 dr., tincture of ipecacuanha 2 dr., glycerin 2 dr., peppermint water to 1 oz. For application to the tongue and gums dilute 3 drops with  $\frac{1}{2}$  dr. of water and use on a piece of gauze.

### **[P1-S1] Collutorium Arsenicalis (T. H.).**

Tincture of ipecacuanha 3 dr., glycerin 5 dr., arsenical solution 5 dr., hydrogen peroxide 5 oz., water to 8 oz. Used diluted with an equal quantity of water for Vincent's angina.

### **Elixir Ipecacuanhæ (B.P.C.).**

**Dose.**—10 to 30 minims (0.6 to 2 ml.).

Contains 5% *v/v* of liquid extract of ipecacuanha in a flavoured basis. Alkaloidal content, 0.1%.

**Extractum Ipecacuanhæ (Fr. Cx.).** Extract the root with 70% alcohol, and evaporate to a firm extract. It contains 6 to 8% *w/w* of total alkaloids.

**Dose.**—Max. single dose 0.3 g.

The water-soluble extractive under the name **Emetin** has been administered in pills or solution as an expectorant in doses of  $\frac{1}{16}$  to  $\frac{1}{8}$  grain (0.004 to 0.006 g.) and as an emetic in doses of  $\frac{1}{2}$  to 1 grain (0.03 to 0.06 g.).

### **Extractum Ipecacuanhæ Liquidum (B.P.).**

**Dose.**— $\frac{1}{2}$  to 2 minims (0.03 to 0.12 ml.); emetic dose, 10 to 30

minims (0.6 to 2 ml.). 2 minims contain  $\frac{1}{2}$  gr. of total alkaloids calculated as emetine.

**Fluidextractum Ipecacuanhæ (U.S.P. XI).** *Average dose.*—Expectorant, 1 minim (0.06 ml.); emetic, 15 minims (1 ml.).

Contains 28 to 33% of alcohol, and hydrochloric acid, and also differs from B.P. liquid extract by being standardised to 2% of ether-soluble alkaloids instead of total alkaloids. *P. Helv. V* has liquid extract containing "at least 2% emetine and cephaeline."

[P1-81] **Ipecacuanha Pulverata (B.P.).** *Syn.* PULVIS IPECACUANHÆ. *Dose.*— $\frac{1}{2}$  to 2 grains (0.03 to 0.12 g.); emetic dose, 15 to 30 grains (1 to 2 g.). 2 grains contain about  $\frac{1}{2}$  gr. of total alkaloids.

Ipecacuanha in fine powder adjusted by admixture with stronger or weaker powder, or lactose, to contain 2% of total alkaloids calculated as emetine, of which not less than two-thirds consists of non-phenolic alkaloids calculated as emetine.

[P1] **Mist. Expect. (N.I.F.).** Ammonium carbonate 3 gr., liquid extract of ipecacuanha  $\frac{1}{2}$  m., camphorated tincture of opium 15 m., water to  $\frac{1}{2}$  oz.

**Mist. Expect. Alk. (N.I.F.).**

Potassium bicarbonate  $12\frac{1}{2}$  gr., ammonium carbonate 3 gr., liquid extract of ipecacuanha  $\frac{1}{2}$  m., liquid extract of squill 2 m., chloroform water to  $\frac{1}{2}$  oz.

**Mistura Ipecacuanhæ Composita (B.P.C.).** *Syn.* MISTURA EXPECTORANS. *Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.).

Contains vinegar of ipecacuanha 24 m. and strong solution of ammonium acetate 15 m. with oxymel of squill, glycerin and chloroform water to 1 oz.

**Mist. Ipecac. c. Scill. (N.I.F.).** Liquid extract of ipecacuanha  $\frac{1}{2}$  m., liquid extract of squill 2 m., concentrated solution of ethyl nitrite  $2\frac{1}{2}$  m. (equivalent to spirit of ethyl nitrite 20 m.), strong solution of ammonium acetate 15 m., water to  $\frac{1}{2}$  oz.

[P1] **Mistura Ipecacuanhæ Salina (Gt. Orm. H.).** (Dose for 1 year old child).

Camphorated tincture of opium 2 m., tincture of ipecacuanha  $1\frac{1}{2}$  m., spirit of nitrous ether 4 m., solution of ammonium acetate 15 m., syrup of tolu 4 m., water to 1 dr.

[P1] **Mistura Pertussis (St. T. H.).** Tincture of belladonna 5 m., tincture of ipecacuanha 5 m., syrup of tolu 30 m., cinnamon water to 1 dr. *Dose.*— $\frac{1}{2}$  to 1 drachm.

[P1-81] **Pigmentum Ipecacuanhæ et Arsenici (R.F.H.).** *Syn.* BOWMAN'S PAINT.

Tincture of ipecacuanha 2 dr., arsenical solution 2 dr., glycerin 2 dr., water to 1 oz. For a child dilute 5 m. to 1 oz. of water and rub into the gums, increase strength if child can be taught to expectorate. For use in pyorrhœa. To be painted on the ulceration. *A drop or two only to be used.*

VINCENT'S STOMATITIS. A local arsenic preparation that is widely used is Bowman's mixture (paint). 5 or 6 drops of this are added to a teaspoonful of water and applied by cotton wool to the mouth and gums.—John Craig, *Practitioner*, ii/1939, 610.

[P1-81] **Pigmentum Arsenicalis (R.N.H.).** Arsenical solution and tincture of ipecacuanha, of each equal parts.

[P1-81] **Pilulæ Ipecacuanhæ cum Scilla (B.P.C.).** *Dose.*—1 or 2 pills. Each pill contains 2 gr. of Dover's powder and  $\frac{2}{3}$  gr. each of squill and ammoniacum (*exempt* [D]).

[P1-81] **Pulvis Ipecacuanhæ et Opii (B.P., U.S.P. XI).** *Syn.* PULVIS OPII ET IPECACUANHÆ COMPOSITUS (I.A.), PULVIS IPECACUANHÆ COMPOSITUS, DOVER'S POWDER, PULVIS OPII COMPOSITUS (P. Ned. V).

**Dose.**—5 to 10 grains (0.3 to 0.6 g.). 10 grains contain  $\frac{1}{10}$  gr. of anhydrous morphine.

Contains 10% each of powdered ipecacuanha and powdered opium, with lactose (*exempt* [D]). Is diaphoretic and anodyne; for an acute catarrh or coryza take 10 gr. at bedtime followed at once by a hot drink and 5 gr. of quinine next morning.

[D-P1-S1] **Poudre d'Ipecacuanha Opiacée** (*Fr. Cx.*). *Max. single dose* 15 grains; *max. during 24 hours* 60 grains. Is the same but has equal parts of potassium nitrate and potassium sulphate *vice* lactose.

[P1-S1] **Pulvis Doveri** (*P. Jap. V*) contains opium 10%, ipecacuanha root 10% and potassium sulphate 80% (*exempt* [D]).

### **Syrupus Ipecacuanhæ (B.P.C.).**

**Dose.**— $\frac{1}{4}$  to 2 drachms (2 to 8 ml.). Contains 50% *v/v* of vinegar of ipecacuanha.

*P.G. VI* and *I.A.* have ipecacuanha tincture 1, syrup 9.

*Fr. Cx.* has "Sirop" 1% of extract made by dissolving extract 1 in alcohol 70% 4, and mixing with syrup to 100; intended as an emetic. That of *I.A.* is not emetic in usual doses.

**Syrupus Ipecacuanhæ (U.S.P. XI).** *Average dose.*—Expectorant, 12 minims (0.75 ml.); emetic, 4 drachms (15 ml.).

Fluid extract of ipecacuanha 7, glycerin 10, syrup to 100.

### **Tinctura Ipecacuanhæ (B.P.).**

**Dose.**—10 to 30 minims (0.6 to 2 ml.); emetic dose,  $\frac{1}{2}$  to 1 ounce (15 to 30 ml.). 30 minims contains about  $\frac{3}{8}$  gr. of alkaloids.

Prepared with 5% *v/v* of liquid extract in a glycerin-alcohol-water medium and contains 0.1% *w/v* of alkaloids. *B.P. Add. I* requires the addition of 1.65% *v/v* (1 m. per dr.) of acetic acid. It is the same strength as Vinum Ipecacuanhæ (*B.P.* '14), which was prepared with sherry. The *B.P.* requires the tincture to be dispensed when the Vinum is prescribed.

*Fr. Cx.*, *P.G. VI*, *P. Belg. IV*, *P. Hung.* and *I.A.* include a tincture (10%) made by percolation of the root with alcohol 70%. *P.G. VI* is standardised to contain 0.194% of emetine.

**Trochisci Ipecacuanhæ (B.P.C.)** contain  $\frac{1}{4}$  gr. (0.015 g.) in each, with simple basis.

[P1] **Trochisci Morphine et Emetini** (TROCHISCI TUSSIS) contain morphine  $\frac{1}{10}$  gr. with emetine  $\frac{1}{10}$  gr. In bronchial asthma.

[P1] **Unguentum Ipecacuanhæ et Crotonis.** Pulvis Ipecacuanha 1, Lini-mentum Crotonis 1, Adeps Benzoinatus 2. A powerful counter-irritant, rubbed on the skin of epigastrium relieves gastralgia.

[P1] **Alcresta Tablets of Ipecac** (*Lilly, London*). Uncoated tablets representing an adsorption compound of ipecac alkaloids with a form of aluminium silicate. The compound passes through the stomach unchanged and liberates the alkaloids in the intestinal tract. Each tablet contains the alkaloids from 10 gr. of ipecacuanha (*U.S.P. XI*).

[P1] **Ipecopan** (*Sandoz, London*). Malted tablets, each containing 2.5 mg. of the hydrochlorides of the total alkaloids of opium, and 0.5 mg. of emetine hydrobromide. *Dose.*—1 to 2 tablets thrice daily. For treatment of coughs.

[P1-S1] **Emetina.** *Syn.* IPECINE, METHYLCEPHAËLINE.

$C_{29}H_{46}O_4N_2 = 480.3$ . *Dose.*— $\frac{1}{12}$  to 1 grain (0.005 to 0.06 g.).

A white powder darkening on exposure. In the stable neutral salts the bases are combined with *two* equivalents of acid. Basic salts also exist.

**Soluble** in water 1 in 600 at 15.5°, 1 in 900 at 40°. Soluble also in ether, alcohol, chloroform and fixed oils. Insoluble in essential oils.

1 gr. in 6 dr. of olive oil has been given as an enema for amœbic dysentery.

[P1] **Emetol** (*Martindale, London*). A solution of emetine base 1 gr. in 2 dr. (8 ml.) of olive oil, for rectal use in amœbic dysentery. *Dose*.—2 drachms are added to 4 or 6 dr. of ether and 8 oz. (230 ml.) of olive oil for use.

[P1-S1] **Emetine Hydrobromide**.  $C_{20}H_{40}O_4N_2 \cdot 2HBr \cdot 4H_2O = 714.2$ .

*Dose*.—As for hydrochloride, *q.v.* for details.

White crystalline salt. Soluble about 1 in 70 only of water, hence the hydrochloride should be prescribed in preference. The addition of a little hydrobromic acid does not affect solubility.

[P1-S1] **Emetinæ Hydrochloridum** (*B.P., P. Jap. V, P.G. VI*).  $C_{20}H_{40}O_4N_2 \cdot 2HCl \cdot 7H_2O = 679.4$ .

*P. Ned. V* has "varying quantity" of water. *P. Helv. V* has "about 4H<sub>2</sub>O." *Fr. Cx.* 5H<sub>2</sub>O. *P. Ital. V* allows 20% and *F.E. VIII* 19% of moisture. *P. Belg. IV* is anhydrous.

*Dose*.— $\frac{1}{2}$  to 1 grain (0.03 to 0.06 g.) by injection,  $\frac{1}{100}$  to  $\frac{1}{2}$  grain (0.0006 to 0.0025 g.) *per os* as an expectorant, but larger doses, e.g.,  $\frac{1}{2}$ , 1 grain are given in enteric coated tablets or pills in amœbic dysentery. As an emetic *per os*  $\frac{1}{2}$  to 1 grain (0.005 to 0.01 g.) has been given. Intravenously  $\frac{1}{2}$  to 1 grain in 5 ml. of normal saline has been given, but its use by this route is not recommended.

*P. Helv. V* has max. single dose 0.1 g. and max. daily dose 0.2 g.

**Soluble** about 1 in 9 in water, but this is not permanent at 15.5°—it is safer to use 20 parts of water at least. The addition of hydrochloric acid throws out the acid salt which is less soluble. Also soluble in alcohol 90% and chloroform, but insoluble in ether.

Injections made with distilled water are less irritant than those made with normal saline. Solutions in ampoules stand sterilising.

**Toxic Effects.** Emetine is a protoplasmic poison acting on all tissues, but appearing to have a selective action on the heart muscle. The effective dosage of emetine seriously overlaps the toxic range and excessive dosage is followed by diarrhoea, nausea, vomiting, depression, peripheral neuritis and cardiac irregularity. It should be used with caution in all cases where the myocardium is damaged, and it is advisable that the patient remain in bed during a course of emetine treatment, and that a careful watch be kept on the pulse-rate, the drug being withheld if this shows a definite increase. According to Chopra, its use is not contraindicated in pregnancy.

Emetine is only slowly excreted and continuous use leads to *cumulative action*. The consensus is that under no circumstances should more than twelve injections of 1 gr. each be given in one course, which may be repeated after an interval of three or four months.

**CUMULATIVE POISONING.** The premonitory signs of poisoning, for which a most careful daily examination is urged to avoid disaster, are:—(1) alimentary; persisting nausea, return of diarrhoea; (2) urinary; oliguria, azotæmia, slight albuminuria; (3) circulatory; grave hypotension, increased cardiac response to effort. The appearance of any one of this triad calls for immediate suspension of

emetine. Established poisoning, which terminates fatally in 25% of cases in which it appears (16 deaths among 66 cases reported in the literature), is manifested by sensory and motor indications of a polyneuritis of the lower or of all four limbs and grave cardiac insufficiency. 0·8 g. is the maximum total dose to be taken in a month, followed by six weeks' suspension of emetine treatment. In adults it is best to give either an intensive course of 0·08 g. of emetine hydrochloride daily for 5 days, followed after 4 days intermission by 0·06 g. daily for 4 days, or a modified course of 0·06 g. daily for 5 to 7 days. Both courses to be followed by six weeks' suspension of emetine treatment, arsenicals being administered meanwhile. In the acute stage of amœbiasis subcutaneous injection is advised; in chronic cases the double iodide of bismuth and emetine, or Auremetine, are given in capsules.—C. Mattei, per *Trop. dis. Bull.*, 1939, 301.

**Antidotes.** Treat as for poisoning by ipecacuanha, *see* p. 655.

**Uses.** The most important use of emetine is in the treatment of amœbic dysentery, especially in the early acute stage. When actual symptoms of dysentery are present the amœbæ are numerous and in full activity and are amenable to the action of emetine. The reason is that the gut in these conditions is hyperæmic, and emetine circulating in the blood will have ready access to the amœbæ. The cases most resistant to treatment are the indeterminate group which get relapse after relapse and fail to react to any drug. In these patients there is superficial ulceration or even considerable thickening and fibrosis of the gut, the amœbæ are walled in, and it becomes difficult for emetine to reach them. It is for this reason that emetine therapy is so frequently a failure in the carrier condition. The respective merits of emetine and surgery in amœbic liver abscess have been widely discussed; according to Chopra, the only indication for surgical interference in this condition is in the presence of bacteria in the aspirated fluid.

Emetine has also been used successfully in a variety of other conditions, *e.g.*, bilharziasis, Guinea worm, and oriental sore. In bilharziasis it is especially indicated in patients who are intolerant to antimony and in young children in whom it is difficult to find a vein. Six daily intramuscular injections of 1 gr. each are given, followed by an interval of six days, and then a second series of six injections. In children, doses of  $\frac{1}{2}$  gr. are often sufficient. In the treatment of oriental sore injections of  $\frac{1}{4}$  gr. are given locally.

Injections of  $\frac{1}{2}$  to 1 gr. of emetine hydrochloride are often effective in arresting hæmoptysis.

A solution of the hydrochloride,  $\frac{1}{2}$  gr. in 8 oz. of water, has been advocated as a mouth-wash in pyorrhœa.

**Treatment of Amœbic Dysentery.** Treatment usually consists of a combination of hypodermic or intramuscular injections of emetine hydrochloride with oral administration of one of the less irritant compounds such as emetine bismuth iodide or the periodide. The injections are made twice daily, an average dose being  $\frac{1}{2}$  gr. each time until 10 to 12 gr. has been given. Intramuscular injections are preferable to hypodermic, as they are less painful and irritant. The treatment is only successful in about one third of the cases treated. Re-treatment with equal or larger amounts is rarely successful.

From observations on the use of emetine in 554 cases of amoebiasis over a period of 15 years at the Mayo Clinic, it seems hardly justifiable to discard its use, though it should be re-emphasised that in the total dose of 0.65 g. in two weeks, it is employed only to control acute manifestations of the disease and to give the patient prompt relief, but not with the idea of continuing the drug to bring about a cure.—P. W. Brown, *J. Amer. med. Ass.*, ii/1935, 1321.

It is now recognised that emetine possesses so great a therapeutic hazard in dosage required for effectiveness in amoebiasis that its routine clinical use in this disease is no longer justified. It has recently been demonstrated *in vitro* that amounts of emetine which are directly lethal for amoebae are much greater than the body tissues can tolerate. It is a fact that clinically safe doses are not always sufficient to rid the patient of this infection, and that amounts in excess of 10 gr. total may produce permanent cardiac damage. The use of this alkaloid should be confined to amoebic hepatitis or abscess and to complicated amoebiasis requiring surgical intervention, since other less harmful drugs are now available for the average uncomplicated case.—H. A. Anderson, *J. trop. Med. (Hyg.)*, 1935, 271.

Emetine is effective only in acute and subacute amoebic dysentery and should be used only in these conditions. It is of practically no use in chronic cases and in carriers, and in bacillary dysentery its use is a confession of ignorance.—A. Viswanathan, *Indian med. J.*, 1939, 304.

In acute amoebic dysentery emetine is given in one grain doses intramuscularly up to a maximum of 9 to 12 gr. over a period of 10 days, by which time all the acute symptoms will have disappeared. When the acute symptoms have subsided E.B.I. is given by the mouth in a maximum dose of 3 gr. daily for 10 to 12 days. This line of combined treatment rarely gives rise to relapses.—K. N. Murthi, *Indian med. J.*, 1939, 298.

AMOEBC LIVER ABSCESS. Aspiration and emetine injection are the methods of choice in the treatment of liver abscess, but it is further advisable to clear up the infection in the bowels with 20 to 30 gr. of ipecacuanha or with E.B.I. internally, so as to prevent relapses.—K. N. Murthi, *Indian med. J.*, 1939, 310.

#### EMETINE INJECTIONS IN CONJUNCTION WITH ARSENIC ORALLY.

Acetarsol 4 gr. twice daily is given for a week or 10 days in conjunction with daily injections of emetine hydrochloride 1 gr.

At the Mayo Clinic, if the patient has not received anti-amoebic treatment recently he is given 0.065 g. of emetine hydrochloride subcutaneously, twice daily for three days. After an interval of a week 0.043 g. of emetine is given twice daily for three more days. With the institution of the emetine, Treparsol 0.25 g. is administered orally with each meal for four days. If there is no intolerance to arsenic, two more such courses are prescribed, with intervals of ten days between the courses. If the patient is quite ill he is kept in bed for the first few days. Obviously, the diet may need to be bland and simple if there is much dysentery, but within 24 to 48 hours a full and generous diet is begun. A rich, high-vitamin diet has a profound influence on the healing of amoebic ulceration. Hepatic involvement may subside, but if there is a large collection of broken-down material, aspiration preferably, or occasionally open drainage, may be required. If stool tests are positive following this regimen, three courses of chiniofon are prescribed: 3 g. orally per day for a week, and repeated for two more such courses with a week's interval between courses. If diarrhoea is increased, the daily dose is decreased, thereby prolonging each course. Failure after this would indicate a course of 1 injection of arspenamine weekly for 6 weeks, and 1 dr. (3.88 g.) of bismuth subnitrate from 3 to 6 times daily during the period. A "cure" should not be regarded as having been attained until three faecal specimens monthly, obtained preferably after a saline purge, are negative over a period of six months.—P. W. Brown, *J. Amer. med. Ass.*, ii/1935, 1319.

#### EMETINE INJECTIONS IN CONJUNCTION WITH BISMUTH ORALLY (JAMES AND DEEKS).

Emetine hydrochloride is injected hypodermically in doses of  $\frac{1}{2}$  to 3 gr. to the limit of tolerance and bismuth subnitrate ("Panama bismuth") is given orally, a heaped teaspoonful (180 gr.) in a tumbler of water every 3 hours night and day in severe cases.

In chronic cases continue for 2 to 3 months after convalescence with 3 or 4 doses daily. Cyanosis and tachycardia may occur but have been stated to be due to impurities in the bismuth subnitrate.

**References to the use of Emetine in other conditions.**

**BRONCHOPNEUMONIA** in children. Though not a specific, it is of value, the febrile period is shortened and the stomach is left free from irritation by expectorants. *Daily hypodermic injection*—up to 4 years,  $\frac{1}{4}$  grain: 4 to 10 years  $\frac{1}{2}$  grain: 10 to 15,  $\frac{1}{2}$  grain. Discontinue if no definite results after 8 injections.—C. R. Wilson, *Brit. med. J.*, i/1928, 845.

**GASTRIC ULCER.** Over 400 cases of gastric and duodenal ulceration treated by intravenous injections; relief complete in each case in periods ranging from 3 days to a week. 1 grain of the salt is dissolved in 6 ml. of treble distilled water and 1 injection into the median basilic or cephalic vein is given on alternate days until 6 have been administered, followed by an interval of a week, when the injections can be repeated. Injections given on an empty stomach and the patient should be kept on a bland salt-free diet during treatment, alcohol in any form being strictly prohibited.—A. E. Olpp, *Med. Rec.*, 1934, 472.

**PULMONARY SUPPURATION.** Emetine 1 gr. daily for 8 to 12 days, preferably combined with strychnine, of benefit. In some cases dramatic results, in others of no value, but never known to do harm.—A. J. Scott Pinchin and H. V. Morlock, *Lancet*, ii/1930, 842, *Practitioner*, ii/1931, 345.

**[P1-81] Emetinæ et Bismuthi Iodidum (B.P.). Syn. E.B.I.**

**Dose.**—1 to 3 grains (0.06 to 0.2 g.) (= approximately 1 gr. of emetine, or about 60 gr. of ipecacuanha) constitutes the average daily dose, given in cachets, tablets, pills or capsules on an empty stomach last thing at night. Twelve doses are given in succession to make up the course. A total of 60 to 70 gr. (4 to 4.6 g.) may be necessary in some cases. If nausea and vomiting are produced, a sedative such as phenobarbitone  $\frac{1}{2}$  to 1 gr., or tincture of opium 10 to 20 m., should be given previously.

A brick-red powder containing 25 to 28% of emetine and 18 to 21% of Bi (1 g. of emetine and bismuth iodide is equivalent to approximately 0.4 g. of emetine hydrochloride).

**Soluble** in acetone, insoluble in water and alcohol. In contact with dilute acids it is slightly decomposed but not dissolved. Is dissolved with decomposition in alkalis and strong acids.

**Uses.** Introduced in the belief that it would not be acted upon by the stomach and that the emetine would be liberated in the intestine. Is considered effective in the treatment of chronic cases and of carriers. The treatment is drastic, but it is claimed to result in a cure in 70 to 80% of cases. Its administration is sometimes combined with injections of emetine. When once a patient has resisted three courses of emetine bismuth iodide it is no use persisting with it.

It is important to observe certain precautions while giving this drug. It is given at bed-time, 4 hours after the last meal of the day, and nothing must be taken after. Any saliva flowing from the mouth should not be allowed to be swallowed. During treatment the patient should remain in bed on a milk diet. Alcohol should be avoided.—K. N. Murthi, *Indian med. J.*, 1939, 298.

**[P1-81] Emetinæ Periodidum. Syn. E.P.I.**

$C_{29}H_{40}O_4N_2I_6 = 1241.9$ .

**Dose.**—The average dose is 2 grains (0.12 g.) thrice daily for 15 days in capsules. Doses as high as 5 grains of the periodide, i.e.,  $1\frac{1}{2}$  grains of emetine, have been given.



A dark purple crystalline powder containing about 38.7% of emetine and 61.3% of iodine. It is obtained by precipitation of an emetine salt with a solution of iodine.

**Soluble** readily in acetone, slightly soluble in alcohol and chloroform, insoluble in water. Practically insoluble in dilute acids.

**Uses.** This drug is the least toxic of the emetine preparations, and as much as 120 gr. has been given over 20 days without toxic symptoms. It causes less vomiting and nausea than emetine and bismuth iodide. In amoebic dysentery it is given in 2 gr. doses thrice daily for 15 days in capsules, one capsule of ox bile, 5 gr., being given simultaneously together with emetine hydrochloride 1 gr. by injection or emetine in oil *per rectum* daily for 6 days. It is also valuable in schistosomiasis, and for other indications for treatment with emetine.

**SCHISTOSOMIASIS.** The oral use clears up the urine of children intensely infected with *S. hamatobium* as quickly and with almost as great certainty as emetine hydrochloride subcutaneously, and without risk. 1 grain of the periodide thrice daily for 15 days was given.—R. M. Gordon, *Brit. med. J. Erit.*, ii/1926, 76.

For tropical use, it is suggested, a preparation of emetine periodide in dried milk (1 grain in 2 drachms, i.e., 8 g.) will be of value. **Directions.**—Two heaped teaspoonfuls in 3 ounces ( $\frac{1}{4}$  cupful) of warm water. The majority of the children apparently successfully treated in 1926 were found to be passing live ova in 1930, but owing to the high degree of infection in the district it was impossible to say whether these were cases of relapse or reinfection.—R. M. Gordon and E. P. Hicks, *Ann. trop. Med. Parasit.*, Oct. 22, 1930.

Relatively safe, but may cause vomiting unless patients are kept in bed on strict diet.—F. G. Cawston, *Brit. med. J.*, i/1929, 890.

[P1-S1] **Auremetine** (*Martindale, London*). A combination of the periodides of emetine and auramine, containing 28% of emetine, 16% of auramine and 56% of iodine, for the treatment of amoebic dysentery. It occurs as a maroon-coloured insoluble powder. Does not cause nausea, vomiting or purging. It is administered in capsules containing 1 gr., 4 times daily for 10 or 15 days, and the administration may be combined with that of acetarsol and bismuth subnitrate as for emetine hydrochloride.

92% of cases treated by the method "responded," i.e., the patient regained his health, lost all clinical signs and symptoms of his disease (including sigmoidoscopic findings), his stools were negative on repeated examination. It is impossible to guarantee permanent cure of chronic amoebic dysentery. Auremetine has given some gratifying and more hopeful immediate results than any other essayed.—J. Graham Willmore, *Proc. R. Soc. Med.*, Nov., 1928.

Combined treatment with Auremetine, bismuth, and acetarsol, has stood the hardest tests and stands first in general usefulness among all the remedies at hand, being the least toxic and the most widely applicable of them all.—Otto Wüner, *J. trop. Med. (Hyg.)*, 1928, 207.

**SCHISTOSOMIASIS** in a child of 16 successfully treated with Auremetine. Live ova disappeared from urine in 24 days. Total dose 47 grains. No vomiting or ill-effects.—R. M. Gordon and E. P. Hicks, *Ann. trop. Med. (Hyg.)*, Oct. 22, 1930.

**Cephaeline.**  $C_{28}H_{35}O_4N_2 = 466.3$ .

**Dose.**— $\frac{1}{12}$  to  $\frac{1}{8}$  grain (0.005 to 0.01 g.).

White silky needles becoming yellow on exposure to light.

**Soluble** in alcohol, chloroform, benzene, caustic alkali solutions. Is a more powerful emetic than emetine. Its action is exerted slowly, and it should be given orally.

By methylation it is converted into emetine.

**Cephaeline Hydrochloride.**  $C_{28}H_{38}O_4N_2 \cdot 2HCl = 539.2$ .

*Dose.*—As for the base. Has been given as an emetic.

**Sedatussin** (*Lilly, London*). Cephaeline hydrochloride  $\frac{1}{10}$  gr., sodium benzoate 4 gr., tincture of sanguinaria 40 m., syrup of squill 48 m., syrup of tolu 60 m., menthol g.s. Cough syrup.

**Acalypha** (*B.P.C.*). *Syn.* INDIAN ACALYPHA, MUKTA-JHURI. The fresh or dried entire plant, *Acalypha indica* (Euphorbiaceæ). A gastro-intestinal irritant. Has been used as a substitute for ipecacuanha.

**Adhatoda** (*B.P.C.*). *Syn.* MALABAR NUT LEAVES, VASAKA. The leaves of *Adhatoda Vasica* (Acanthaceæ). Used as an expectorant in the form of liquid extract, syrup, or tincture, also smoked for asthma.

**Angelice Radix** (*B.P.C.*).

*Dose.*—10 to 30 grains (0.6 to 2 g.).

The dried rhizome and roots of *Angelica Archangelica* (Umbellifereæ). Contains 0.3 to 1% of volatile oil. The powder and an infusion (1 in 20) have been administered for their stimulant, diaphoretic and expectorant properties. The seeds (*Angelice Fructus B.P.C.*) have similar properties. *Fr. Cx.* includes leaf and root.

**Calotropis** (*B.P.C.*). *Syn.* MUDAR. *Dose.*—Expectorant, 3 to 10 grains (0.2 to 0.6 g.); emetic,  $\frac{1}{2}$  to 1 drachm (2 to 4 g.). Dried root-bark of *C. procera* and *C. gigantea* (Asclepiadaceæ). Used in the East instead of ipecacuanha. *Tinctura Calotropis, dose.*— $\frac{1}{2}$  to 1 drachm, 1 in 10.

**Eriodictyon** (*B.P.C.*). *Syn.* YERBA SANTA.

*Dose.*— $\frac{1}{2}$  to 1 drachm (1 to 4 g.). The dried leaves of *Eriodictyon glutinosum* (Hydrophyllaceæ). Expectorant and bitter tonic. Has been used in asthma, chronic bronchitis and phthisis. Is administered as a liquid extract, 1 in 1, prepared with alcohol 25%, *dose*—15 minims. The liquid extract greatly reduces the bitterness of mixtures containing quinine or other bitter drugs.

*Eriodictyon* (*U.S.P. XI*) is from *E. Californicum*.

**Fluidextractum Eriodictyi** (*U.S.P. XI*). *Average dose.*—15 minims (1 ml.). 1 in 1, prepared with a mixture of alcohol 95% 4 parts and water 1 part.

The action of liquid extract of eriodictyon in removing the bitter taste of solutions of quinine or strychnine is due to the presence of resinous matter which adsorbs the alkaloid.—Fantus, Dyniewicz and Dyniewicz, *J. Amer. pharm. Ass.*, 1933, 323.

**Grindelia** (*B.P.C., Fr. Cx.*).

The dried leaves and flowering tops of the "Gum Plant," *Grindelia camporum* (Compositæ). The involucre, and often the leaves, are coated with resin, 20% or more, to which the medicinal action is due.

*Uses.* For the spasmodic attacks which occur in asthma, whooping-cough and bronchitis, and given in heart disease to slow and regulate the pulse.

**Extractum Grindeliæ Liquidum** (*B.P.C.*). 1 in 1.

*Dose.*—10 to 20 minims (0.6 to 1.2 ml.) at the onset of a paroxysm of asthma, repeated every hour, in sweetened water or milk.

A 1 in 10 dilution has been used in dermatitis due to the poison ivy, *Rhus toxicodendron*.

**Extractum Grindeliæ.**

*Dose.*—2 to 3 grains (0.12 to 0.2 g.) 3 times a day.

Prepared by evaporating the alcoholic percolate.

[*P*] **Grindeline** (*Oppenheimer, London*). *Dose.*—1 to 2 drachms in water every 2 to 4 hours. Containing liquid extract of grindelia 15 m., potassium iodide 2 gr., glyceryl trinitrate  $\frac{1}{100}$  gr., liquid extract of euphorbia 20 m. in each drachm.

[P1] **Mist. Grindeliæ (N.I.F.).** Liquid extract of grindelia 10 m., ethereal tincture of lobelia 7½ m., tincture of belladonna 5 m., liquid extract of liquorice 10 m., mucilage of acacia 30 m., chloroform water to ½ oz.

[P1] **Spiritus Grindeliæ Compositus.**

*Dose.*—½ to 2 drachms (4 to 8 ml.) in water every 2 to 4 hours while attack of asthma lasts.

Liquid extract of grindelia 15 m., sodium iodide 2 gr., solution of glyceryl trinitrate ½ m., tincture of euphorbia pilulifera 20 m., spirit of chloroform to 1 drachm.

**Holarrhena (B.P.C.).** *Syn.* CONESSI BARK, TELICHERRY BARK, KURCHI OR COORCHI. The bark of the stem and root of *H. antidysenterica* (Apocynaceæ), a small deciduous tree found throughout India. The plant, as also *H. Congolensis* from the Congo, contains conessine,  $C_{12}H_{20}N$ . This alkaloid has strong inhibitory action on amœbæ—equal to that of emetine. It is 50% less toxic than the latter. Conessine salts can be given *per os* and intravenously, but subcutaneously they produce necrosis at site of injection. The bark has remarkable effect in amœbic dysentery. Suggested dose of powdered bark 2 to 5 grains. A liquid extract 1 = 1 has been used with good result in daily doses of 6 to 8 drachms.

Antidysenteric value compares favourably with any other remedy in vogue and depends on use of entire seed or bark. Recommended daily dose of 60 to 120 grains of powdered bark in 3 or 4 portions.—*Lancet*, i/1928, 39; see also T. A. Henry and H. C. Brown, *ibid.*, 108.

Comparative treatment of 154 cases of amœbic dysentery with Alcresta Ipecac, emetine injections, emetine injections plus bismuth *per os*, emetine and bismuth iodide, Yatren, Stovarsol and kurchi bark, showed that the last two gave the best results, the ratio of probable cures to failures in each of these cases being 1:1.1.—R. Knowles, *per Lancet*, ii/1928, 714. Total kurchi bark alkaloids used with success in amœbiasis—2 grain doses intramuscularly or liquid extract orally.—*Per Med. Annu.*, 1931, 17.

Compared with emetine, kurchi is rather slow in action and does not produce that dramatic effect often experienced with emetine in acute cases. But in other respects it is superior to emetine. It is non-toxic, non-emetic, and is capable of oral administration, and a daily dose of the liquid extract totalling 2 to 4 gr. of the alkaloid per day continued for a fortnight, is an efficient and dependable amœbicide.—A. Viswanathan, *Indian med. J.*, 1939, 304.

**Kurchi Bismuth Iodide.** *Dose.*—4 grains twice daily for 10 days in amœbiasis. In acute amœbic infections nine ½- to 1-grain doses of the total kurchi bark advised.—H. W. Acton and N. R. Chopra, *Med. Annu.*, 1931, 17.

Intramuscular injections of 2 gr. of kurchi alkaloid as effective as emetine, but painful. Kurchi-bismuth-iodide compares favourably with corresponding emetine compound in 10 gr. doses twice daily, preceded half an hour beforehand by 60 gr. of sodium bicarbonate and 40 gr. of sodium citrate, for 10 days or longer. Second course not recommended.—H. W. Acton and R. N. Chopra, *Indian med. Gaz.*, 1932, 6.

**Phytolacca (B.P.C.).** *Syn.* POKE ROOT.

*Dose.*—1 to 5 grains (0.06 to 0.3 gr.).

The root of *Phytolacca decandra* (Phytolaccaceæ) containing a bitter resin. Is emetic, purgative and mildly sternutatory. Has been given in chronic rheumatism, and used as a local application in mammitis and mumps.

Phytolaccin, *dose*—1 to 5 grains, is the dried extractive.

**Antidotes.** Empty stomach by emetic or stomach tube. Give stimulants, *e.g.*, aromatic spirit of ammonia, ½ dr. in water. Digitalis may be necessary, and morphine, ½ gr. hypodermically, for pain.

**Sanguinaria** (B.P.C.). *Syn.* BLOOD ROOT. *Dose.*—1 to 5 grains (0.06 to 0.3 g.). The dried rhizome of *S. Canadensis* (Papaveraceæ). Expectorant in chronic bronchitis. Has been given as a 10% tincture, *dose.*—15 minims.

A resinoid extractive, sanguinarin, *dose.*— $\frac{1}{4}$  to 1 grain, is made.

**Simaruba** (B.P.C.). *Dose.*— $\frac{1}{4}$  to  $\frac{1}{2}$  drachm (1 to 2 g.). The dried root-bark of *S. amara* (Simarubaceæ). Used as a bitter, and as an astringent in dysentery. Administered as a decoction (1 in 20).

**Decoctum Simarubæ et Punice Granati.** Add simaruba bark, pomegranate fruit rind and gum arabic of each 15 g. to a litre of water, and boil down to  $\frac{1}{2}$  litre. *Dose.*—30 ml. 3 or 4 times daily. For the treatment of dysentery. The quantities and the ingredients have been varied from time to time.

## JALAPA

(with IPOMŒA, etc.)

*B.P., Fr. Cx., P. Jap. V, P. Helv. V, P. Dan.*

*Syn.* BRYONE NOIRE, MECHOACAN NOIR, VERA CRUZ JALAP.

The dried tubercles of *Ipomæa purga* (*syn. Exogonium purga*) (Convolvulaceæ). A powerful purgative producing watery stools; it is apt to gripe, and must be avoided if the bowels are inflamed. Used to reduce dropsy of Bright's disease, and to relieve uræmia. When Jalapa is prescribed Jalapa Pulverata is to be dispensed.

**Jalapa Pulverata** (B.P.).

*Dose.*—5 to 20 grains (0.3 to 1.2 g.).

Jalap in fine powder adjusted with exhausted jalap or lactose to contain 10% of resin.

**Pulvis Jalapæ Compositus** (B.P.).

*Dose.*—10 to 60 grains (0.6 to 4 g.).

Powdered jalap 30% with ginger 10% and potassium acid tartrate.

**Tinctura Jalapæ** (B.P.C.).

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.). Contains 1.5% of resin.

**Tinctura Jalapæ Composita** (B.P.C.).

*Dose.*— $\frac{1}{4}$  to 1 drachm (2 to 4 ml.). Contains 1 in 12 $\frac{1}{2}$  of jalap with scammony resin and turpeth.

**Tinctura Jalapæ Composita** (*Fr. Cx.*). *Syn.* EAU-DE-VIE ALLEMANDE. Prepared by macerating jalap 8 g., turpeth 1 g., scammony 2 g., in alcohol 60% for 10 days.

**Jalapæ Resina** (B.P.C., *Fr. Cx., P. Jap. V, P.G. VI, P. Ital. V, F.E. VIII, P. Belg. IV, P. Helv. V and P. Dan.*).

*Dose.*—1 to 5 grains (0.06 to 0.3 g.).

Contains two glucosidal resins, about 90% convolvulin (*syn. JALAPURGIN*), soluble in alcohol, but insoluble in ether, together with about 10% soluble in ether and in alcohol. The latter, orizabin or jalapin (Mayer), the principal constituent of spurious jalap (*Ipomæa simulans*), is identical with scammonin from ipomœa. It is cheaper and less active. B.P.C. requires not less than 85% of ether-insoluble resins.

A jalap resin, known as *Regina de Batata de Purga*, and extracted from the tubercle of *Convolvulus Operculatus*, is extensively used in Brazil. It possesses the same properties as the official jalap, but is practically devoid of any subsequent constipating action. Dose.—0.25 to 2 g.—*Chem. & Drugg.*, i/1925, 854.

**Jalapinum (B.P.C.).**

Dose.—1 to 5 grains (0.06 to 0.3 g.).

The ether-insoluble portion of the resin obtained from jalap, occurring as a white odourless powder with acrid taste, m.p. about 155°. **Soluble** in alcohol, glacial acetic acid and ethyl acetate, insoluble in ether and water, slightly soluble in chloroform. Is considered less active than jalap resin.

It should be distinguished from the substance known in Germany as jalapin, which is the ether-soluble portion of jalap resin.

**Ipomœa (B.P.).** *Syn.* ORIZABA JALAP ROOT, MEXICAN SCAMMONY ROOT.

Dose.—5 to 20 grains (0.3 to 1.2 g.).

The dried root of *I. orizabensis* (Convolvulaceæ). A powerful purgative very similar in its action to jalap and containing up to about 20% of resin.

**Scammonia Resina (B.P.).** *Syn.* RESINA IPOMŒÆ (U.S.P. X), RESINA SCAMMONIÆ MEXICANÆ (Fr. Cx.).

Dose.— $\frac{1}{2}$  to 3 grains (0.03 to 0.2 g.).

**Soluble** in alcohol 90%, insoluble in water, wholly or partly soluble in ether. The ether-soluble portion of scammony resin is known as scammonin. Purgative in obstinate constipation, producing copious watery evacuation in a few hours. Does not act until reaching the duodenum.

**Pulvis Scammonia Compositus (B.P.C.).**

Dose.—10 to 20 grains (0.6 to 1.2 g.). Scammony resin 50% with jalap and ginger.

**Pilula Scammonia Composita (B.P.C.).**

Dose.—1 or 2 pills. Contain 1 gr. each of scammony resin, jalap resin and curd soap, and  $\frac{1}{2}$  gr. of ginger.

**Scammonium (B.P.C.).** *Syn.* RESINA SCAMMONIÆ (Fr. Cx.), VIRGIN SCAMMONY, dose.—5 to 10 grains (0.3 to 0.6 g.), is the gum-resin obtained from Levant scammony root (*Convolvulus Scammonia*). It occurs in blackish pieces giving an emulsion with water. It resembles scammony resin in its action.

**Cambogia (B.P.C., P. Helv. V, P. Austr., Fr. Cx.).** *Syn.* GOMME GUTTE.

Dose.— $\frac{1}{2}$  to 2 grains (0.03 to 0.12 g.). *P. Helv. V* max. single dose 3 grains approx., max. in 24 hours 10 grains. Yellow gum-resin from *Garcinia Hanburyi* (Guttifera) growing in Siam. A powerful purgative, and may cause severe griping. Will expel tapeworm. Is rarely now given alone. Indian gamboge, from *G. Morella*, is similar.

**Kaladana (B.P.C.).** *Syn.* PHARBITIS SEEDS.

Dose.—30 to 45 grains (2 to 3 g.). The dried seeds of *Ipomœa hederacea* (Convolvulaceæ). Purgative and anthelmintic.

**Pulvis Kaladana Compositus and Tinctura Kaladana** are prepared in the same way as the corresponding preparations of jalap, and are used instead of them in India and the East.

**Kaladana Resina.** Dose.—2 to 8 grains (0.12 to 0.5 g.).

Useful hydragogue, used as a substitute for jalap resin in India and the East.

**Leptandra** (B.P.C.). *Syn.* BLACK ROOT, CULVERS ROOT.

*Dose.*— $\frac{1}{2}$  to 1 drachm (1 to 4 g.).

The dried rhizome and roots of *Veronica virginica* (Scrophulariaceæ). Cholagogue, reputed to act without irritating the bowels. Often combined with podophyllin or euonymin.

**Extractum Leptandræ** (B.P.C.). *Syn.* LEPTANDRIN.

*Dose.*— $\frac{1}{2}$  to 2 grains (0.03 to 0.12 g.). A dry extract.

[P1] **Tabellæ Leptandræ Compositæ** (B.P.C.). *Syn.* TABELLÆ LAXATIVÆ COMPOSITÆ, VEGETABLE LAXATIVE TABLETS. *Dose.*—1 to 3 tablets.

Contain compound extract of colocynth 1 gr.,  $\frac{1}{2}$  gr. each of leptandra, jalap resin, resin of podophyllum, dry extract of hyoscyamus and extract of taraxacum, and oil of peppermint.

**Turpethum** (B.P.C., *Fr. Cx.*). *Syn.* INDIAN JALAP. *Dose.*—5 to 20 grains (0.3 to 1.2 g.). The dried root and stem of *Ipomœa Turpethum* (Convolvulacææ). Contains 5 to 10% of resin and is used in the East in place of jalap.

## KRAMERIA

(with KINO, CATECHU, etc.)

*B.P., Fr. Cx., P. Helv. V, P. Dan.*

*Syn.* RHATANY ROOT, PERUVIAN RHATANY.

The dried root of *Krameria triandra* (Polygalacææ). Contains about 8% of a tannin. Astringent in relaxed throat. Also used in tooth powders when gums are liable to bleed, and in mouth-washes, also for bleeding from nose and bowels, and for diarrhœa.

The root of *K. argentea*, known as Pará Rhatany, is not official.

**Extractum Kramerizæ Siccum** (B.P., *Fr. Cx.*).

*Dose.*—5 to 15 grains (0.3 to 1 g.). The aqueous percolate evaporated to dryness under reduced pressure.

**Infusum Kramerizæ Concentratum** (B.P.C.).

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.). 1 in 2 $\frac{1}{2}$ .

**Infusum Kramerizæ Recens** (B.P.C.). *Syn.* INFUSION OF RHATANY.

*Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.). 1 in 20.

**Tinctura Kramerizæ** (B.P.).

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.). 1 in 5 of 60% alcohol by percolation.

**Garg. Kramer. Co.** (N.I.F.). Tincture of krameria 3 dr., liquefied phenol 3 dr., glycerin 4 dr., peppermint water to 8 oz. For use dilute one tablespoonful with  $\frac{1}{2}$  pint of warm water.

**Trochiscus Kramerizæ** (B.P.) contains 1 gr. of the dry extract.

[D-P1-81] **Trochiscus Kramerizæ et Cocainæ** (B.P.) contains 1 gr. of the dry extract with  $\frac{1}{2}$  gr. of cocaine hydrochloride.

**Kino** (B.P.C., U.S.P. XI, *P. Helv. V*).

*Dose.*—5 to 20 grains (0.3 to 1.2 g.). U.S.P. XI average dose 8 grains.

The dried juice from the trunk of *Pterocarpus Marsupium* (Leguminosæ). Genuine kino is sometimes difficult to obtain,

and frequently the commercial article is inferior, and undoubtedly derived from a different source.

Partly *soluble* in cold water, more soluble in hot water and alcohol 90%, nearly insoluble in ether. Contains 70 to 80% of kinotannic acid. Astringent for diarrhoea, and as Trochisci for relaxed condition of the throat. The powder is also insufflated to check epistaxis.

[P1-81] **Pulvis Kino Compositus (B.P.C.).**

*Dose.*—5 to 20 grains (0.3 to 1.2 g.).

Kino 75%, powdered opium 5%, and cinnamon 20% (*exempt* [D]).

**Tinctura Kino (B.P.C.).**

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.). 1 in 10.

The tincture may gelatinise, due to enzymes, on storage.

*Incompatible* with mineral acids and alkalis and with substances precipitable by the tannin it contains.

**Tinctura Kino (U.S.P. XI).** *Average dose.*—30 minims (2 ml.).

1 in 5; double the strength of the U.S.P. X tincture.

**Kino Eucalypti (B.P.C.).** *Syn.* RED GUM, GUMMI EUCALYPTI.

*Dose.*—5 to 20 grains (0.3 to 1.2 g.).

An exudation from *Eucalyptus rostrata* (Myrtaceæ), and other species. About 80% of it is soluble in cold water, and about 90% in alcohol 90%. Used in diarrhoea, and relaxed throats, and as astringent in dentistry, cuts, etc. As astringent in hæmorrhage and in relaxed conditions of the larynx and trachea, it is used mixed with an equal weight of starch. As a suppository, 5 gr. in oil of theobroma may be used.

To be distinguished from the common Australian or Botany Bay kino, said to be from *E. resinifera*.

**Extractum Kino Eucalypti Liquidum (B.P.C.).** *Syn.* EXTRACTUM GUMMI RUBRI LIQUIDUM.

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.). 1 in 4.

**Gargarisma Kino Eucalypti (B.P.C.).** Liquid extract of kino eucalyptus 6.25% v/v.

**Tinctura Kino Eucalypti (B.P.C.).** *Syn.* TINCTURA GUMMI RUBRI.

*Dose.*—15 to 40 minims (1 to 2.6 ml.). 1 in 4.

**Trochisci Kino Eucalypti (B.P.C.).** *Syn.* RED GUM LOZENGES; EUCALYPTUS GUM LOZENGES. Contain 1 grain.

**Bela (B.P.C.).** *Syn.* BAEL FRUIT. The fresh or dried half-ripe fruit of *Aegle Marmelos* (Rutaceæ). Mild astringent. The fresh fruit is useful in dysentery and in dyspepsia.

**Extractum Belæ Liquidum (B.P.C.).** *Dose.*—1 to 2 drachms (4 to 8 ml.). 1 in 1.

**Buteæ Gummi (B.P.C.).** *Syn.* BENGAL KINO. Obtained from incisions in the stem of *Butea frondosa* (Leguminosæ). Used in the East in place of kino.

**Catechu (B.P., P. Helv. V).** *Syn.* CATECHU PALLIDUM, GAMBIR.

*Dose.*—5 to 15 grains (0.3 to 1 g.).

A dried aqueous extract of the leaves and young shoots of *Uncaria gambir* (Rubiaceæ). Soluble in water to the extent of about 50%. Astringent in diarrhoea.

**Mist. Catechu Co. (N.I.F.).** Powdered catechu 10 gr., aromatic powder of chalk 15 gr., chalk 15 gr., chloroform water to  $\frac{1}{2}$  oz.

**Pulvis Catechu Compositus (B.P.C.).** *Dose.*—10 to 60 grains (0.6 to 4 g.). 1 in 2 $\frac{1}{2}$ , with kino, krameria, cinnamon and nutmeg.

**Tinctura Catechu (B.P.).** *Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

1 in 5 of alcohol 45% with cinnamon 1 in 20.

**Trochiscus Catechu (B.P.C.)** contains 1 grain. For relaxed throat.

**Catechu Nigrum (B.P.C.).** *Syn.* CUTCH, CACHOU DE PÉGU (*Fr. Cx.*), CATECHU (*Fr. Cx.*).

*Dose.*—5 to 15 grains (0.3 to 1 g.).

An extract prepared from the heartwood of *Acacia Catechu* (*Leguminosæ*) used for the same purposes as catechu.

**Rhus (B.P.C.).** *Syn.* RHUS FRUCTUS, SUMACH, SUMAC BERRIES.

*Dose.*—10 to 30 grains (0.6 to 2 g.).

The dried fruits of *R. Glabra* (*Anacardiaceæ*). Astringent and reputed diuretic. The liquid extract (1 in 1) and decoction (1 in 20) have been used in gargles.

**Rhus Toxicodendron (Anacardiaceæ).** *Syn.* POISON OAK, POISON IVY LEAVES. Tincture. *Dose.*—2 to 15 minims. Imported from North America, prepared from fresh leaves 1, alcohol 2. It is much employed in homeopathic medicine in the treatment of subacute and chronic rheumatism, chronic skin affections, and other conditions. It may irritate the stomach and bowels. The poisoning by the "Toxicodendrol" contained takes the form of an itching, burning, erythematous and herpetiform rash. Swab skin with 5% potassium permanganate—recovery rapid. A 1 in 10 dilution of liquid extract of grindelia is also effective. A 5% ferric chloride solution in 50% glycerin, washed freely on skin will act as a preventive.

A vanishing cream base (potassium stearate) containing 10% of sodium perborate or potassium periodate was found to be an effective preventive against poison ivy dermatitis. It is recommended that it be rubbed well into the skin of the arms and face before exposure. After a few hours it should be washed off and a fresh portion applied before further exposure. The cream must be freshly prepared and not used after 2 to 3 weeks, since it deteriorates rapidly.—L. Schwartz, L. H. Warren and F. H. Goldman, *Publ. Hlth Rep., Wash.*, 1940, 55, 1327.

**Coto (B.P.C.).** *Syn.* PARACOTO.

*Dose.*—1 to 8 grains (0.06 to 0.5 g.), in powder, 4 to 6 times a day.

A bark of unknown botanical origin imported from Bolivia; probably from a species of *Nectandra*. Has been used in cholera, and the diarrhoea of phthisis, for night sweats, and for gout and rheumatism.

**Extractum Coto Liquidum (B.P.C.).** 1 = 1 of bark.

*Dose.*—5 to 15 minims (0.2 to 1 ml.).

**Tinctura Coto (B.P.C.).** *Dose.*—10 to 30 minims (0.6 to 2 ml.). 1 in 10.

**Mistura Anti-choleraica (Royal Coll. Phys., Form II).**

Aromatic sulphuric acid 15 minims, compound tincture of camphor 30 minims, compound tincture of chloroform, tincture of coto, of each 20 minims, syrup of orange flower 1 drachm, peppermint water to 1 ounce. *Dose.*—1 ounce every 3 or 4 hours.

**Rosæ Petalum (B.P.C.).** *Syn.* RED-ROSE PETALS (*Fr. Cx.*). The petals of the red or French rose, *Rosa gallica*. *Flos Rosæ* (*P. Helv. V*) is from *R. gallica* or *R. centifolia*. Mildly astringent.

**Confectio Rosæ Gallicæ (B.P.C.),** *syn.* CONFECTION OF ROSES, consists of the fresh petals beaten to a paste with sucrose.

**Infusum Rosæ Acidum Concentratum (B.P.C.).**

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

About 1 in 5. Approximately 8 times the strength of the fresh infusion.

**Infusum Rosæ Acidum Recens (B.P.C.).**

*Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.). 1 in 40, with 1 in 80 of dilute sulphuric acid.



**Syrupus Rosæ (B.P.C.).**

**Dose.**— $\frac{1}{4}$  to 1 drachm (2 to 4 ml.). A solution of sucrose in an acidified aqueous infusion of the petals.

**Rosæ Centifoliæ Petalum, syn. PALE-ROSE PETAL (Fr. Cx.),** is obtained from the cabbage or Provence rose, *Rosa centifolia*.

**Rosæ Fructus (B.P.C.). Syn. HIPS.** The fresh ripe fruits of the dog rose, *Rosa canina* (Rosaceæ) and other closely allied species.

**Confectio Rosæ Caninæ (B.P.C.), syn. CONFECTION OF HIPS,** consists of the hips deprived of their achenes and beaten to a pulp with sucrose. Occasionally used as a pill excipient.

**Salix (B.P.C.). Syn. WILLOW BARK.** The bark of *S. alba* and other species. Contains tannin and salicin. Has been employed as a bitter and astringent.

**Extractum Salicis Nigræ Liquidum (B.P.C.). Dose.**— $\frac{1}{4}$  to 1 drachm (1 to 4 ml.). 1 in 1.

## LIGATURES AND SUTURES

Surgical ligatures and sutures are materials used in surgery for tying and stitching respectively. They fall into two main divisions, those which are absorbed by the body and become replaced by a ring of living tissue, and those which are not absorbed. The absorbable, non-irritating type are few in number, catgut and kangaroo tendon being the only ones in common use. The non-absorbable type act as foreign bodies when introduced into living tissue, and set up irritation leading to their isolation by the formation of a fibrous capsule, or their ejection through a stitch-abscess. This class includes horsehair, silk, silkworm gut and Japanese synthetic gut.

The properties essential to a satisfactory surgical ligature or suture are sterility, tensile strength commensurate with gauge, and good keeping qualities. It is in the attempts to fulfil these requirements that very considerable difficulties are met with, the prolonged heating or chemical action to which it is necessary to expose some materials to ensure sterility often having a detrimental effect on the tensile strength. Because of this difficulty of ensuring a satisfactory sterile substance, surgical ligatures and sutures were brought within the scope of the Therapeutic Substances Act, 1925, by the Therapeutic Substances Regulations 1931 (amended by S.R. and O. 1937, No. 767). The regulations control the manufacture and importation for sale of any ligature or form of binding material prepared from the gut or any tissue of an animal, and offered for sale for use in surgical operations on the human body. The substances to which the Regulations apply are catgut, kangaroo tendon and horsehair, and the chief requirements include a licence to manufacture granted by the Ministry of Health for England and Wales, the Department for Health for Scotland, or the Ministry of Home Affairs for Northern Ireland, use of approved processes for manufacture and sterilisation and subjection to prescribed bacteriological tests of not less than one per cent. of material from every batch manufactured.

Every container must bear on it, or on a label enclosed within it, the name of the substance and its source, for example, "surgical

ligature (catgut)," the manufacturer's licence number and a distinctive batch number. The Regulations also control the labelling of non-sterile surgical ligatures and sutures, not offered or intended to be offered for sale as sterile, the containers of which must bear the following words written or printed in indelible red ink:—"non-sterile surgical ligature (suture)—not to be used for operations upon the human body unless efficiently sterilised." Otherwise non-sterile material is outside the scope of the Regulations. The control exercised under the Act has raised considerably the standard of sterility of ligatures and sutures on sale in this country, and it is unfortunate that the preparation of sterile ligatures and sutures in hospitals for use in the operating theatre is outside this control. Hospitals are recommended to use only materials manufactured under a licence issued under the Therapeutic Substances Act, unless they are certain that the same precautions are observed in the preparation of and the same tests applied to their own product as are required under the Act and Regulations.

**Catgut** is almost exclusively prepared from the small intestine of lambs, preferably that of young lambs, and consists of the submucous cellular coat, the other layers being scraped away during the course of manufacture. The raw material for catgut manufacture is heavily infected with a variety of micro-organisms, among which there may occur pathogenic anærobcs, so that sterilisation becomes a matter of primary importance.

The intestines, after removal, are stroked free from fæces and immediately salted or frozen. In the factory the blocks of frozen gut are thawed out, thoroughly washed, soaked in weak alkali to make them soft and supple, and then split longitudinally into ribbons. The ribbons are scraped to free them from the unwanted layers, leaving the *submucosa* only. Sometimes a preliminary sterilising or inhibiting process is carried out at this stage by soaking the ribbons in a disinfectant solution. Gut treated in this way but not subjected to a sterilising process after spinning, is often sold as "internally sterilised" catgut, and is purchased by hospitals and similar institutions, who subject it to a final sterilising action before use. As this material is not sold as sterile and ready for use, it falls outside the scope of the Therapeutic Substances Regulations, and great care should be taken when buying "internally sterilised" catgut to ascertain that the material has been through an efficient sterilisation process, as the final treatment that it will receive in the hospital often effects very little more than surface sterilisation, and the use of infected material of this type has undoubtedly led to wound infection.

After splitting, the ribbons are fastened together in twos, threes, or fours with string loops, the number used depending upon the gauge of the catgut desired, and with the aid of a mechanical device a definite number of twists is given. The "spun" string is stretched and dried under tension, the product being "raw" catgut. The dried raw catgut is polished with glass paper or similar material and graded according to thickness.

There is, unfortunately, no recognised gauging standard for surgical catgut in U.K., and each manufacturer sets his own, often with varying results. A typical scale is given below, in which the gauge number is compared with the diameter of the gut and the standard wire gauge.

Catgut No.	Diameter	Standard Wire Gauge No.	Catgut No.	Diameter	Standard Wire Gauge No.
	<i>In.</i>			<i>In.</i>	
8/0	0.010	33	0	0.018	26
6/0	0.0116	31	1	0.020	25
4/0	0.0136	29	2	0.022	24
3/0	0.0149	28	3	0.024	23
2/0	0.0164	27	4	0.028	22

At this stage the gut is sometimes submitted to a chemical process for the purpose of hardening the gut and so delaying its absorption by the body. Various substances have been used for this purpose, including potassium dichromate and tannic acid. For example, *Lister's sulphochrome catgut* is prepared by soaking raw catgut for 24 hours in twenty times its weight of "preparing fluid" made by dissolving chromic acid 4, in water 240, adding sufficient sulphurous acid to produce the green colour of chromium sulphate, making up to 480 (by weight) with water, and finally adding a solution of mercuric chloride 2, in water 320. The catgut is dried under tension. Lister considered that sulphochrome catgut does not begin to be absorbed for about ten days, and is then only gradually eroded, retaining considerable firmness to the last. By variations in the treatment to which the gut is submitted, it is claimed that the time of absorption can be controlled, and so-called 10, 20, 30 day catguts are supplied. Such times can only be approximate, since the rate of absorption varies with the type of tissue in which it is embedded, and with the individual.

**Sterilisation.** Production of sterile catgut must from the very nature of its origin and method of manufacture prove difficult. The presence of such pathogenic organisms as tetanus and anthrax is almost certain, and as during the manufacture they become embedded in the strands by the twisting of the ribbons, it becomes a matter of great importance to find a process which will penetrate the tissue and kill any spores present without affecting the physical characters of the material, including its suppleness and tensile strength. It is essential that the tensile strength shall be good on both the length and the knot, and it may readily be lost during the sterilisation process.

Many processes have been used for producing sterility, including treatment with phenol in oil, mercuric chloride, mercuric biniodide, silver compounds, essential oils, iodine and heat. All

have objectionable properties in some degree or another, some are not sporicidal, others do not penetrate, whilst a number affect the tissue of the gut and render it practically useless. The most effective chemical sterilising agents are hydrogen peroxide and iodine. The former, owing to its swelling effect on "spun" gut, is seldom employed by itself, but is generally used for treating the wet gut as a preliminary to the action of iodine.

**Iodine Treatment.** Iodine is the most practical sterilising agent, as it possesses great penetrating power and may be relied upon to produce a sterile gut with good physical properties. The process consists of immersing the catgut under tension in an aqueous solution containing iodine 1%, potassium iodide 2%, potassium iodate 0.25%, glycerin 5 to 10%, for eight to nine days, until it has absorbed 12% of its weight of iodine. The process is said to depend upon the formation of nascent hydriodic acid, which is of great sporicidal value, from the reaction of iodine and organic matter. The potassium iodate is added to prevent damage to the catgut by the excessive formation of acid, while the glycerin maintains its suppleness and increases the tensile strength on the knot. The next step is to remove the excess of free iodine by replacing the iodine solution with a sterile bleach containing sodium thiosulphate. The strings are then thoroughly washed and dried by dehydration with spirit or other means. Under aseptic conditions, the gut is cut to the required lengths, coiled, tubed, and the tubes filled with an alcoholic solution of iodine diluted with just enough water to allow the iodine to exert a germicidal effect without waterlogging the catgut. This removes any slight contamination picked up during the bleaching, washing, drying and tubing processes. After an appropriate time, the iodine solution is replaced by the final alcoholic tubing fluid, and the tubes are sealed.

**Heat Treatment.** Heat is probably the most efficient and reliable agent provided the physical properties of the catgut remain unimpaired. Heating catgut in air renders it hard and brittle, whilst heating it in a moist atmosphere ruins it immediately. Accordingly the raw catgut is first thoroughly dried by placing it already cut to the required length, coiled and tubed, in warm ovens. Immediately after drying the tubes are placed in an autoclave containing an organic fluid such as toluene or xylene, and gradually heated. The temperature is usually maintained somewhere between 150° and 165° for several hours, and at the end of this time the autoclave is allowed to cool slowly. The tubes are removed, the final tubing fluid added under aseptic conditions, and the tubes sealed.

Tubing fluids vary in their composition, but are usually alcoholic solutions of different chemicals containing, if necessary, the correct amount of water to recondition heat-treated catgut. It may be emphasised here that alcohol used in any process should be sterilised by filtration before use, since spores can remain unharmed by immersion in it for long periods.

**Tests for Sterility.** All ligatures and sutures manufactured under licence must be subjected to prescribed tests for sterility. The Regulations specify that not less than one per cent. of each batch shall be examined by the following procedure. The container is opened and the sample removed aseptically. It is drained and placed in sterile water and incubated at 37° for 24 hours. The sample is then transferred aseptically to a sterile aqueous solution of sodium thiosulphate 1%, and sodium carbonate 1%, and again incubated at 37° for 24 hours. This solution is intended to remove iodine used in the manufacture of the ligature or suture. If any other substance has been used instead of iodine, the manufacturer must obtain the approval of the licensing authority to substitute an alternative procedure. This part of the test is of great importance, and its neglect in the past has undoubtedly led to the reliance which is wrongly placed on such disinfectants as mercuric chloride, mercuric biniodide, essential oils, etc., which, while

having insufficient penetrating power to ensure the internal sterility of catgut are bacteriostatic enough to prevent growth of organisms in culture media.

After the second incubation the sample, without further washing, is divided into two portions and tested for the presence of aerobic and anaerobic organisms by incubating in suitable media for twelve days at 37°. Only if negative results are obtained from the test may the ligatures or sutures be passed for sale.

The tests prescribed in the *U.S.P. XI Supp. II* for the sterility of surgical gut are similar except that the material is also tested for moulds and yeast, and all cultures showing no growth at the end of the tests are themselves tested for absence of bacteriostatic agents which may have been accidentally transferred.

The terms "boilable" and "non-boilable", which are often applied to catgut, indicate those tubes of material which can and cannot be boiled before opening for the purpose of sterilising the outside of the tube. Such a process can have no effect on the sterility of the gut and may damage its physical properties. It is preferable, therefore, to wash the tube with a germicidal solution.

**Chorda Chirurgicalis** (*U.S.P. XI Supp. II*). *Syn.* SURGICAL GUT; SURGICAL "CATGUT," "CATGUT" SUTURE.

It consists of sterile gut prepared from the submucous connective tissue of the small intestine of the sheep. The monograph includes the following four types depending upon the treatment they have undergone to increase their resistance to digestion. Type A, plain or untreated; Type B, mild treatment; Type C, medium treatment; Type D, prolonged treatment. Each type may be supplied as "boilable" or "non-boilable." The monograph controls length, diameter, tensile strength on the straight pull and over a surgeon's knot, sterility, labelling, etc.

References to surgical catgut:—

W. Bullock, L. H. Lampitt and J. H. Bushill, *Med. Res. Council Special Rep.* No. 138, 1929.

W. Dalrymple Champneys, *Proc. R. Soc. Med.*, 1936, 29, 465.

E. J. Holder, *Surgical Sutures and Ligatures* (E. & S. Livingstone), 1939.

T. J. Mackie, Report to the Scottish Board of Health, 1928.

T. J. Mackie, Report to the Department of Health for Scotland, 1929.

*Pharm. J.*, ii/1936, 254.

**Kangaroo tendon** consists of the tendons dissected out from kangaroo tails. They form very stout material about 10 inches in length and, like catgut, are absorbable in a wound. They are used for suturing large wounds in heavy muscle. Sterilisation is difficult but can be carried out as for catgut.

**Non-absorbable Ligatures.** The greatest use for this type of material is for suturing skin, but some surgeons prefer silk to catgut for internal operations although the silk will probably remain *in situ*. This preference is, in many cases, due to the fact that silk can be readily sterilised in the operating theatre.

Non-absorbable sutures should preferably have a smooth surface, be impermeable to water, resilient, and easy to remove after the healing of the wound. They are often coloured to contrast with the skin.

**Black horsehair** occurs in hanks, the threads being up to 28 inches in length. It is smooth and impermeable. It is occasionally used for small skin wounds, but is generally not very satisfactory as it is inclined to be brittle, particularly on the knots, whilst the gauge gradually decreases from the base to the tip. It may be sterilised by thoroughly washing in neutral soap solution and boiling or autoclaving.

**Silkworm gut.** *Syn.* CRINA (*Fr. Cx.*). It has the same composition as ordinary silk, but a much wider gauge. Instead of being spun by the living silkworm it is extracted by the fingers from worms which have been killed. It is manufactured chiefly in Spain for this special purpose.

Silkworm gut occurs in hanks of 50 threads, the threads having an effective length of 10 to 14 inches. The gauges may be very fine, fine, medium, and stout, but being hand-prepared, the gauge may vary in the same thread. Silkworm gut is often supplied dyed in different colours, each colour representing a particular gauge, so that the surgeon can distinguish a mixture of threads of different gauges on the sterilising tray. Sterilisation may be carried out as for horsehair. It is employed as a substitute for catgut in deep-seated operations.

**Japanese synthetic gut** consists of silk thread specially surfaced and hardened by treatment with agar or some similar substance. It is a very stout material, very supple and smooth, and is supplied in a large variety of gauges. It occurs in lengths up to 40 yards. It may be sterilised as for horsehair and silkworm gut.

**Silk.** Ordinary silk thread slightly waxed is employed for long skin suturing, and very fine silk for suturing blood vessels, divided nerves and fascia. It is not advisable to use it where definite sepsis occurs, as it is liable to absorb contamination. It may be sterilised as for horsehair.

**Nylon**, a synthetic super polymer, is marketed by *I.C.I. (Plastics) Ltd., Welwyn*, as non-absorbable surgical sutures. It forms into filaments of great strength, toughness and elasticity, which are uniformly even and smooth. The sutures are more easily withdrawn than natural silkworm gut sutures. They are of solid section and consequently non-capillary. Nylon does not soften in water or steam at the highest temperatures normally used for sterilising, and it is unharmed by any of the usual sterilising agents or antiseptic solutions, except phenols and strong mineral acids. Available in 14-inch lengths.

## LINUM

(with PSYLLIUM, etc.)

*B.P., U.S.P. XI, Fr. Cx., P. Jap. V, P. Helv. V.*

The dried ripe seeds of *Linum usitatissimum* (Linacæ). The seeds contain mucilage and about 30% of fixed oil. Preparations are administered for their demulcent action in the treatment of cough. The seeds, 1 or 2 teaspoonfuls in a tumbler of water, may be taken to increase the bulk of the intestinal contents in the treatment of constipation.

**TOXICOLOGY OF LINSEED PLANT.** Cattle poisoning by linseed flowers is fairly common in Bengal. The results of an investigation into the amount of hydrocyanic acid liberated by the enzyme linase from different parts of the plant showed that flowers after fertilisation (*i.e.*, with immature seeds) were the most potent, as much as 0.69% of HCN being liberated in water and 0.6% in acid. A strong solution of an alkali (sodium carbonate) has been suggested as an antidote in linseed flower poisoning.—K. N. Bagchi and H. D. Ganguli, *Indian J. vet. Sci.*, 1939, 9, 61, per *Analyst*, 1939, 680.

**Infusum Lini** (*B.P.C.*). *Syn.* LINSEED TEA.

*Dose.*—1 to 4 ounces (30 to 120 ml.). About 1 in 30.

**Linum Contusum** (*B.P.*). *Syn.* CRUSHED LINSEED, LINSEED MEAL. Coarsely powdered linseed, freshly prepared. Contains not less than 30% of oil.

**Mucilago Lini** (*B.P.C.*). 1 in 8.

**Oleum Lini** (*B.P., U.S.P. XI, P. Helv. V, P. Dan.*).

*Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.).

A yellowish-brown drying oil expressed from linseed. It thickens on exposure to air. **Soluble** 1 in 40 of dehydrated alcohol, slightly soluble in alcohol 90%; miscible with turpentine, ether, chloroform, carbon disulphide and light petroleum.

**Boiled linseed oil** is linseed oil heated with litharge, magnesium resinate or other "driers" causing the oil to dry more rapidly. It must not be used for linseed oil.

**Fœnum-græcum** (B.P.C., *P. Helv. V*). *Syn.* FœNUGREEK. The seeds of *Trigonella Fœnum-græcum* (Leguminosæ), a herb largely grown in India and Egypt. The seeds contain a large proportion of mucilage and about 5% of oil, and are used chiefly in veterinary medicine.

An Egyptian preparation, *Helba*, is made from fœnugreek—when soaked the seeds swell into a pasty condition and are used for fever, also for diabetes. Seeds which have been allowed to sprout for 3 or 4 days are sometimes preferred and are taken raw, together with unsprouted seeds. A decoction of fœnugreek, an egg-cupful to a pint of water, boiled down to 5 oz., strained and taken cold on an empty stomach, has been used in diabetes.

### **Ispaghula** (B.P.C.).

*Dose.*—45 to 150 grains. Pinkish-brown, boat-shaped seeds of *Plantago ovata* (Plantaginaceæ), containing mucilage and swelling in contact with moisture. Administered internally in intestinal atony, also in chronic diarrhœa, either dry, or as Decoctum Ispaghulæ (1½%) in doses of ½ to 2 ounces.

It has been suggested as a war-time substitute for agar and psyllium.

**Ispaghulæ Testa**, *syn.* ISPAGHULA HUSK, consists of the separated epidermis of the seeds. It is used in the same way as the whole seeds, but is more powerful in its action.

**Psyllium** (B.P.C., *Fr. Cx.*). *Syn. and Prop. Names.* FLEA SEED, ARCOLAX (Roberts, London), PSYLLA (Battle Creek Food Co., Michigan; Coates & Cooper, London).

The dried ripe seeds of *Plantago Psyllium* and of *P. arenaria* (Plantaginaceæ), from Southern Europe. Contain mucilage and are used in constipation, 1 to 4 teaspoonfuls or more being allowed to soak in half a cupful of water until a jelly is produced, the whole then being taken. The 1½% decoction is used in France as a demulcent drink.

**Coréine** (Daniel-Brunet, Boulogne-sur-Seine; Wilcox, JozEAU, London). Pure vegetable mucilage in flakes or granules. *Dose.*—2 teaspoonfuls thrice daily. For constipation.

**I-so-gel** (Allen & Hanburys, London). The dried mucilage of certain tropical seeds in granular form. *Aperient.*

**Sylnasol** (G. P. Searle, Chicago; A. Tate, London). A 5% solution of the fatty acids of a vegetable oil extracted from a seed of the psyllium group for the injection treatment of hernia.

Of 109 cases of inguinal hernia treated and followed up, 32 (29%) had recurrences. The longest time any patient was observed to remain cured was 42 months and the shortest two months, the average period being 14 months. The advantages of injection treatment are its safety, lack of complications, and the fact that the patient remains ambulatory; the chief disadvantages are that it is prolonged and that the recurrence rate is higher than would be expected from expert surgery.—H. K. Sowles and W. H. Shedden, *New Engl. J. Med.*, 1/1940, 753.

**Salep.** *Syn.* TUBERA SALEP (*P. Helv. V, P. Jap. V, P.G. VI, P. Ned. V, P. Belg. IV*).

The dried tubers of *Orchis mascula* and other species of *Orchis* (Orchidaceæ). They are immersed in boiling water on collection and dried. They contain mucilage, and have nutritious and demulcent properties, allaying gastro-intestinal irritation. Mucilage Salep (*P.G. VI, P. Jap. V*) is 1% freshly made. Salep is much sold in the Indian bazaars as an article of diet.

**Ulmus Fulva** (*B.P.C.*). *Syn.* SLIPPERY ELM. The dried inner bark of *U. fulva* (Ulmaceæ). It contains much mucilage and in powder is used as a demulcent in catarrhal affections and in diarrhœa and dysentery. It should be free from starch. Ten grains shaken with an ounce of water should form a thick, jelly-like, fawn-coloured mass. Mixed with hot water, the powder is used as a poultice in abscesses and whitlows. Decoction.—1 in 8. *Dose.*—2 to 4 ounces. Glycogelatin pastilles are prepared containing 2 grains.

It is recommended that steps should be taken to prohibit the sale by retail of sticks of slippery elm bark, owing to its popularity as an instrumental means of criminally terminating pregnancy.—*Report of the Inter-Departmental Committee on Abortion, H.M.S.O., 1939.*

## LITHIUM

Li = 6.94.

Lithium salts have long had a reputation for assisting in the elimination of uric acid, but their effect is probably analogous to that of the corresponding potassium salts. Their introduction into medicine was due to a misconception. Lithium urate being relatively soluble, the lithium salts were introduced as solvents for uric acid, but since the soluble urate cannot exist in the body or in the urine in the presence of sodium or potassium ions, there is no rational foundation for the use of these salts. When given they should be freely diluted.

**Lithii Benzoas** (*B.P.C., Fr. Cx.*).  $C_6H_5COOLi = 128.0$ .

*Dose.*—5 to 15 grains (0.3 to 1 g.).

A light, white, crystalline powder or in scales. Antiseptic and diuretic.

**Soluble** about 1 in 3 of water, about 1 in 15 of alcohol 90%.

**Incompatible** with acids and sodium bicarbonate.

**Lithii Carbonas** (*B.P.C., P. Helv. V, Fr. Cx.*).

$Li_2CO_3 = 73.88$ .

*Dose.*—2 to 5 grains (0.12 to 0.3 g.). Tablets, 5 grains. A white amorphous or minutely crystalline powder.

**Soluble** 1 in 75 of water, 1 in 140 of boiling water, more soluble in water containing carbon dioxide; insoluble in alcohol. Diuretic, thought to increase the alkalinity of the blood.



**Lithii Chloridum (B.P.C.).**  $\text{LiCl} = 42.40$ .

*Dose.*—5 to 10 grains (0.3 to 0.6 g.).

White deliquescent crystals or crystalline powder, with salty taste.

*Soluble* 1 in  $1\frac{1}{2}$  of water, 1 in 30 of alcohol.

**Lithii Citras (B.P.C.).**  $\text{C}_2\text{H}_4\text{OH}(\text{COOLi})_3 \cdot 4\text{H}_2\text{O} = 281.9$ .

*Dose.*—5 to 10 grains (0.3 to 0.6 g.).

White crystalline powder. Diuretic.

*Soluble* 1 in 2 of water, insoluble in alcohol 90%.

**Lithii Citras Effervescens (B.P.C.).**

*Dose.*—1 to 2 drachms (4 to 8 g.). Contains 1 in 20.

**Lithii Guaiacas.**

*Dose.*—5 grains (0.3 g.) in pill twice a day.

Prepared by digesting guaiacum resin in solution of lithium oxide, decanting the solution, evaporating, and scaling it. Contains lithium oxide 1, guaiacum resin 3. For gout and rheumatism.

**Lithii Hippuras.**  $\text{C}_6\text{H}_5 \cdot \text{CO} \cdot \text{NH} \cdot \text{CH}_2 \cdot \text{COOLi} \cdot 2\text{H}_2\text{O} = 221.0$ .

*Dose.*—5 to 20 grains (0.3 to 1.2 g.).

In light, white, minute crystals, soluble 1 in 3 of water. Has been used in gout and rheumatism. Effervescent lithium hippurate contains 5 grains in 1 drachm.

**Lithii Sulphas.**  $\text{Li}_2\text{SO}_4 \cdot \text{H}_2\text{O} = 109.9$ .

*Dose.*—5 to 10 grains (0.3 to 0.6 g.).

White crystals soluble in water and alcohol.

**Lithii Tartras Acidus.**  $\text{CHOH} \cdot \text{COOLi} \cdot \text{CHOH} \cdot \text{COOH} \cdot 1\frac{1}{2}\text{H}_2\text{O} = 183.0$ .

*Dose.*—5 to 20 grains (0.3 to 1.2 g.).

White crystalline powder, used in gouty cases with gum affections.

## LOBELIA

*B.P., Fr. Cx., P. Belg. IV, F.E. VIII, P. Dan., P. Helv. V.*

[P1] "*Alkaloids, the following; their salts, simple or complex:—Lobelia, alkaloids of.*"

[S1] "*Alkaloids, the following; their salts, simple or complex:—Lobelia, alkaloids of, except substances containing less than 0.5 per cent. of the alkaloids of lobelia.*"

[S3] "*Alkaloids—Lobelia, alkaloids of—in preparations for the relief of asthma in the form of cigarettes, smoking mixtures or fumigants; substances containing less than 0.1 per cent. of the alkaloids of lobelia.*"

[S6] "*Alkaloids—Lobelia, alkaloids of—specify proportion as the proportion of any one alkaloid of lobelia that the preparation would be calculated to contain on the assumption that all the alkaloids of lobelia in the preparation were that alkaloid.*"

*Dose.*—1 to 3 grains (0.06 to 0.2 g.).

The dried aerial parts of *Lobelia inflata* (Campanulacæ). Has purgative and emetic properties in large doses, but its chief use is to relax spasm of the bronchi in asthma and bronchitis. It is contained in many anti-asthmatic powders (*vide Pulvis Lobeliæ Compositus*). Large doses are diuretic, cathartic and emetic, and

may cause collapse through medullary paralysis. It should not be employed in the presence of cardiac disease.

**Antidotes.** Treat as for poisoning by nicotine, *see* p. 867.

[P1] **Mistura Lobeliæ et Stramonii Composita (B.P.C.).**

**Dose.**— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.).

Contains potassium iodide 5 gr., and ethereal tincture of lobelia 10 m., with ammonium carbonate and tincture of stramonium in chloroform water to 1 oz.

[P1] **Mist. Lobel. Co. (N.I.F.).** Ethereal tincture of lobelia 10 m., potassium iodide 3 gr., mucilage of tragacanth 30 m., tincture of stramonium 20 m., chloroform water to  $\frac{1}{2}$  oz.

[P1] **Mist. Lobel. Co. (P.M.H.).** Potassium iodide 10 gr., ammonium carbonate 5 gr., ethereal tincture of lobelia 20 m., tincture of ipecacuanha 20 m., spirit of chloroform 5 m., concentrated infusion of senega 60 m., water to 1 oz.

[P1] **Nebula Lobeliæ Composita.** Tinctures of lobelia, belladonna and stramonium, of each 10 m., tincture of ipecacuanha 5 m., sodium nitrite 10 gr., glycerin and rose water to 1 oz.

**Pulvis Lobeliæ Compositus (B.P.C.)** contains equal parts of lobelia, stramonium and tea impregnated with potassium nitrate and oil of anise.

**Pulvis Stramonii Compositus (B.P.C.)** contains stramonium 50%, with lobelia, anise and tea impregnated with potassium nitrate.

The fumes of half a teaspoonful or more to be inhaled six or eight times a day. Himrod's and Potter's Asthma cures and proprietary asthma cigarettes are preparations of similar type (*see* Vol. II).

[P1] **Tinctura Lobeliæ Ætherea (B.P.).**

**Dose.**—5 to 15 minims until nausea occurs.

1 in 5, prepared by percolation with spirit of ether.

**ASTHMA.** The following antispasmodic mixture may be taken at first thrice daily and then, as the attacks diminish in frequency, reduced to morning and evening doses, and finally taken in the evening only: ethereal tincture of lobelia 15 m., tincture of stramonium 15 m., potassium iodide 5 gr., arsenical solution 3 m., camphor water  $\frac{1}{2}$  oz.—Whitla, 8th Edn., 1938.

[P1] **Tinctura Lobeliæ Simplex (B.P.C.).** *Syn.* TINCTURA LOBELIÆ. **Dose.**—10 to 30 minims (0.6 to 2 ml.).

1 in 8 in alcohol 60%. I.A. agreed 10% w/w in alcohol 70%.

[P1-S1] **Lobelinum Hydrochloricum (P.G. VI, P. Belg. IV, P. Helv. V).**  $C_{22}H_{27}O_2N \cdot HCl = 373.7$ .

**Max. dose.**— $\frac{1}{2}$  grain (0.02 g.): *per diem*  $1\frac{1}{2}$  grains (0.1 g.). *P. Helv. V* has  $\frac{1}{8}$  and  $\frac{1}{4}$  grain respectively.

Intravenously  $\frac{1}{8}$  grain (10 mg.) in 1% solution.

A white crystalline powder, **soluble** 1 in 50 of water, 1 in 10 of alcohol; easily soluble in chloroform. **Solutions must not be heated.**

**Used** as respiratory stimulant in emergencies, also in coal gas poisoning and in acute morphine poisoning, but it has only a transient action and repeated injections are necessary.

[P1-S1] **Lobeline.**  $C_{12}H_{17}O_3N = 337.2$ .

A crystalline alkaloid obtained from lobelia. A powerful respiratory stimulant, but should be used cautiously in patients with enfeebled myocardium. Probably more effective combined with a cardiac stimulant. Is usually used as the hydrochloride.

[P1] **Lobelin Ingelheim** (*Boehringer, Hamburg; Zimmermann, London*). Solution of lobeline hydrochloride in 1 ml. ampoules containing  $\frac{1}{10}$  grain (0.01 g.) or  $\frac{1}{20}$  grain (0.005 g.). *Dose.*—Subcutaneously for adults and for older children,  $\frac{1}{10}$  grain; for new-born infants,  $\frac{1}{20}$  grain intramuscularly. The effect sets in after  $\frac{1}{2}$  to 1 minute, but is of short duration. Injections may be repeated every 2 to 4 hours. In particularly urgent cases  $\frac{1}{10}$  gr. may be given by slow intravenous injection, and is effective in 3 to 6 seconds.

## MAGNESIUM

Mg = 24.32.

**Magnesii Carbonas Levis** (*B.P., Fr. Cx., P. Helv. V, P. Dan.*).

*Dose.*—10 to 60 grains (0.6 to 4 g.).

Prepared by boiling together dilute solutions of magnesium sulphate and sodium carbonate. The composition corresponds approximately to  $3MgCO_3 \cdot Mg(OH)_2 \cdot 3H_2O$ .

*Uses.* During their passage through the intestinal tract the magnesium salts are mainly changed to the soluble bicarbonate. Their effects are therefore largely identical, *i.e.*, antacid and mildly laxative, except in the case of the sulphate, which has a cathartic action. The carbonates are less effective as antacids than the oxides, and have the disadvantage of liberating carbon dioxide. The light carbonate is more suitable for mixtures and the heavy variety for powders. The neutralising value of the oxides is more than twice that of the carbonates. For a description of mixtures of carbonates used for the treatment of gastric and duodenal ulcer, see under *Pulvis Bismuthi Compositus*, p. 301.

A paper on the preparation, composition, impurities and uses of magnesium oxides and carbonates.—J. S. F. Gard, *Quart. J. Pharm.*, 1938, 572.

**Mist. Mag. Carb.** (*N.I.F.*).

Sodium bicarbonate 15 gr., light magnesium carbonate 10 gr., chloroform  $\frac{1}{2}$  m., peppermint water to  $\frac{1}{2}$  oz.

**Magnesii Carbonas Ponderosus** (*B.P.*).

*Dose.*—10 to 60 grains (0.6 to 4 g.).

Prepared by mixing boiling concentrated solutions of magnesium sulphate and sodium carbonate, evaporating to dryness and washing out the sulphate. The composition corresponds approximately to  $3MgCO_3 \cdot Mg(OH)_2 \cdot 4H_2O$ .

**Magnesii Carbonas** (*U.S.P. XI*).

*Average dose.*—As antacid 10 grains, as laxative 2 drachms.

Described as a bulky white powder or as light white friable masses. Contains the equivalent of about 41% of MgO.

**Sippy's Powder.**

*Dose.*— $\frac{1}{2}$  to 2 drachms (2 to 8 g.) in water.

No. 1—Magnesium carbonate and sodium bicarbonate equal parts.

No. 2—Calcium carbonate and sodium bicarbonate equal parts.

Sippy's treatment of gastric ulcer (introduced in 1915) consisted in giving large doses of alkalis after, and of belladonna before, the feeds, and by using as the basis of the diet milk and cream. The feeds are given at two or two and half

hourly intervals, an alkaline powder is taken one hour after, and olive oil or belladonna before the feeds. The treatment is now little used in this country.—*Cf. Maclean's Powder*, p. 302.

**Liquor Magnesii Bicarbonatis (B.P.).** *Syn.* FLUID MAGNESIA. *Dose.*—1 to 2 ounces (30 to 60 ml.).

A colourless liquid saturated with carbon dioxide and containing not less than 2.5% *w/v* of  $Mg(HCO_3)_2$ , equivalent to about 7½ grains of magnesium carbonate in 1 oz.

It can be made in a Sparklet syphon as follows:—Add a boiling solution of magnesium sulphate 40 g. in water 200 ml. to a cold solution of sodium carbonate 50 g. in water 200 ml.; boil until carbon dioxide is removed, collect the precipitate on a calico strainer, wash until free from sulphate, suspend in 400 ml. of water and transfer to a "C" size Sparklet syphon. Discharge a bulb of gas into the liquid, shake and allow to stand for 6 hours. Discharge a second bulb, shake and allow to stand for 18 hours.—*G. R. Gibbon, Pharm. J., ii/1934, 403.*

### **Magnesii Citras.**

A white, odourless, crystalline substance obtained by the interaction of citric acid and a magnesium salt.

**Soluble** in water. It is best used in the form of effervescent magnesium citrate, or as solution of magnesium citrate as a purgative or cooling drink.

**Magnesium Citricum Siccum (Fr. Cx.)** is prepared by dissolving citric acid 100, in water 30, and adding the solution to magnesium carbonate 60, in a porcelain dish. The mixture is well stirred, slowly dried and powdered.

**Liquor Magnesii Citratis (B.P.C.).** LIMONADE CITRO-MAGNESIENNE (Fr. Cx.).

*Dose.*—3½ to 10 ounces (100 to 500 ml.), or more.

A solution containing magnesium citrate, saturated with carbon dioxide and flavoured with lemon.

**Liquor Magnesii Citratis (U.S.P. XI).** *Average dose.*—7 ounces (200 ml.).

Prepared by dissolving magnesium carbonate in a hot solution of citric acid, adding syrup and heating to boiling point, adding oil of lemon mixed with talc and filtering while hot into a strong bottle; after diluting to the required volume and cooling, potassium or sodium bicarbonate is added, the bottle securely stoppered, and kept on its side in a cool place, preferably in a refrigerator. It must be dispensed in bottles holding 200 or 350 ml.

[P1] **Mistura Magnesii et Belladonnæ (C.X.H.).** *Syn.* MISTURA GASTRICA. Light magnesium carbonate 10 gr., bismuth carbonate 10 gr., tincture of belladonna 7½ m., sodium citrate 15 gr., peppermint water to 1 oz. For hyperacidity and peptic ulcer. To be taken 3 or 4 times a day, the last dose being increased to 1½ or 2 oz.

**Magnesii Hydroxidum (B.P.C.).** *Syn.* MAGNÉSIE HYDRATÉE (Fr. Cx.).  $Mg(OH)_2 = 58.3$ .

*Dose.*—10 to 60 grains (0.6 to 4 g.), or more. Usually administered as Mistura Magnesii Hydroxidi (*vide infra*).

Prepared by decomposition of magnesium sulphate 24½ with sodium hydroxide 8 in solution, the precipitate being washed free from sulphate and dried at a low heat.

According to the *Fr. Cx.*, calcined magnesia is boiled with 20 to 30 times its weight of distilled water 20 minutes. Dry as much as possible by collecting on calico and finally at 50° until it no longer loses weight. Thus prepared, magnesium hydroxide contains 31% of water.

It dissolves more freely in dilute acids than calcined magnesia and is preferred to the carbonates as an antacid since no carbon dioxide is liberated. It is a recognised antidote in arsenical poisoning.

[P2] **Lotio Magnesii Hydroxidi et Phenolis** (*St. Mark's H.*).

Phenol 15 gr., zinc oxide 30 gr., calamine 15 gr., glycerin 30 m., rose water 60 m., mixture of magnesium hydroxide to 1 oz.

**Mistura Magnesii Hydroxidi (B.P.).** *Syn.* CREAM OF MAGNESIA, CREMOR MAGNESIÆ.

*Dose.*—1 to 4 drachms (4 to 16 ml.). Four drachms contains the equivalent of about  $12\frac{1}{2}$  gr. of magnesium oxide.

An aqueous suspension of hydrated magnesium oxide containing the equivalent of about 8.25% of  $Mg(OH)_2$ . Antacid without evolving carbon dioxide.

On standing in contact with ordinary glass bottles magnesium hydroxide suspensions increase in alkalinity and develop a bitter taste. This can be prevented by using hard glass bottles or by adding 0.1% of citric acid.—E. C. Billheimer and F. W. Nitardy, *J. Amer. pharm. Ass.*, 1936, 36.

*Uses.* In indigestion, dyspepsia, acidity, rheumatism, and as an alkaline mouth-wash. A useful antidote in case of poisoning by mineral acids.

**Magma Magnesiae (U.S.P. XI).** Contains 7 to 8.5% of  $Mg(OH)_2$ . No method of preparation is given, and the solution may contain 0.1% of citric acid to minimise its action on glass, and 0.05% of volatile oil for flavouring purposes.

**Alkagen Tablets (Allen & Hanbury, London).** Contain magnesium hydroxide 5 gr. and peppermint oil  $\frac{1}{4}$  m. *Dose.*—1 to 3 with water. For acidity, flatulence, etc. Lozenges and granules containing glucose are also available.

**Lactomagnesia (Crookes Laboratories, London).** An antacid and laxative containing 10% colloidal magnesium hydroxide.

[P1] **Sedogastrine (Bengal, London).** Magnesium hydroxide, calcium carbonate, sodium and calcium phosphates, and conium, in granules and tablets for hyperacidity, dyspepsia, etc.

**Magnesii Lactas.**  $(C_2H_5OH \cdot COO)_2Mg \cdot 3H_2O = 256.4$ .

*Dose.*—15 to 60 grains (1 to 4 g.). White crystalline powder. Soluble 1 in 30 of water; insoluble in alcohol 90%.

A mild laxative. Useful in some cases as a hæmostatic where calcium salts do not seem to act. A dose of 30 grains usually reduces time of coagulation of the blood 30%, e.g., from 2 to  $1\frac{1}{2}$  minutes. The salt can be made extemporaneously by the dispenser, if prescribed in a mixture, from magnesia 1, with lactic acid about 5. The large dose of the bulky powder, if ordered in that form, is inconvenient to take.

**Magnesii Oxidum Leve (B.P., Fr. Cx.), syn. MAGNESIA LEVIS, MAGNESII OXIDUM (U.S.P. XI), and Magnesii Oxidum Ponderosum (B.P.), syn. MAGNESIA PONDEROSA.**  $MgO = 40.32$ .

*Doses.*—As for the carbonates. *U.S.P. XI* has average dose as antacid 4 grains, as laxative 45 grains.

These are prepared from the respective carbonates by exposure to a dull red heat. Antacid, antilithic, diuretic, laxative.

Magnesia should never be prescribed as compressed tablets since these do not dissolve and may form the nucleus of calculi.

**Magnesii Phosphas (B.P.C.).** *Syn.* TRIBASIC MAGNESIUM PHOSPHATE (*U.S.P. XI Supp. II*). *Dose.*— $\frac{1}{4}$  to 1 drachm (1 to 4 g.).

A white, slightly gritty powder consisting of a hydrated tribasic

phosphate containing about 30% of combined water. Products containing more water are liable to become fungoid.

**Used** as an antacid. Does not produce systemic alkalisation. Has laxative action.

**Magnesii Sulphas** (*B.P.*, *U.S.P.* XI, *Fr. Cx.*, *P. Jap. V*). *Syn.* EPSOM SALTS, *SEL ANGLAIS* (*P. Belg. IV*), *SEL D'ANGLETERRE*, *SEL DE SEDLITZ* (*P. Helv. V*, *P. Dan.*).  $\text{MgSO}_4 \cdot 7\text{H}_2\text{O} = 246.5$ .

**Dose.**— $\frac{1}{2}$  to 4 drachms (2 to 16 g.).

Death following ingestion of 57 g. Care should be exercised as toxicity may result without death—idiosyncrasy may exist and the average dose may be toxic. If toxicity does occur use calcium salts subcutaneously or intravenously.—H. S. Thatcher, *J. Amer. med. Ass.*, ii/1928, 1185.

In colourless crystals with a saline bitter taste.

**Soluble** 10 in 13 of water—measuring 18.5 (*B.P.* gives 1 in 1 $\frac{1}{2}$ ); also soluble 1 in 1.1 of glycerin, solution taking place very slowly. For extemporaneous preparation dissolve 70 g. in 15 ml. of boiling water and add glycerin to 120 ml. Sparingly soluble in alcohol.

**Incompatible** with Soda Tartarata, alkali carbonates and bicarbonates unless in dilute solution. With potassium or ammonium bromide concentrated solutions give a precipitate of the double sulphate.

**Uses.** Taken internally, magnesium sulphate is a very efficient evacuant, producing watery stools with little or no griping. Its use as a purgative is indicated whenever prompt action is called for, when it is desired to cleanse the bowel of poisonous material, to relieve cerebral congestion or œdema, or to obtain watery evacuations in ascites or other forms of dropsy. An injection directly into the duodenum, by means of a duodenal tube, of an ounce of a 24% solution causes relaxation of the sphincter of the gall-bladder and permits of the collection of the bile for study, or, when this does not appear, indicates obstruction of the gut (Meltzer-Lyon Test); this procedure has also been employed for evacuation of the gall-bladder in cholecystitis. In cases of injury to the brain dehydration by the use of magnesium sulphate *per rectum*, 3 ounces in 6 fluid ounces of warm water, repeated four-hourly, gives marked relief.

Because of its osmotic and anæsthetic action it is widely employed as a local dressing, in the form of a saturated solution, in various inflammatory conditions, such as sprains, bruises, arthritis, orchitis, cellulitis, insect bites, epididymitis, erysipelas, etc., or as a paste in carbuncles, boils, etc. (*see* Morison's Paste).

When introduced into the circulation it acts as a depressant to the central nervous system and intravenous injections of 10 to 25 ml. of a 10% solution are used to control eclamptic convulsions. Intraspinal injections of 2 to 6 ml. of a 25% solution have given good results in tetanus, and in chorea hypodermic or intramuscular injections of 5 ml. of a 20 to 25% solution have been found of value.

**ANGIOSPASM.** Cases of intermittent claudication, endarteritis obliterans, Buerger's disease, migraine, spasm of the brachial artery, acute pulmonary œdema, angina pectoris, coronary thrombosis and cerebral angiospasm have all been treated with varying success by magnesium sulphate intravenously. The

patient lies on a couch with head and shoulders slightly raised and a solution of magnesium sulphate and glucose is slowly injected. The dose is 5 to 10 ml. of a 20% solution and an equal volume of 10% to 40% glucose. About half a minute after commencement of injection the patient feels intense heat all over the body. Treatment usually given twice weekly. Magnesium sulphate probably relaxes vascular spasm by direct action on the vasomotor centre of the brain.—N. Pines, *Lancet*, i/1933, 577.

**DEAFNESS.** Hot baths containing 1 lb. of magnesium sulphate are sometimes effective in a minority of chronic cases. To be used with caution in elderly people. 10 minutes' immersion enough. Exhausting.—J. Adam, *Brit. med. J.*, i/1931, 621.

**ECLAMPSIA.** 5 to 10 ml. of 25% solution intramuscularly after each convulsion until controlled. It is not used in coma. Give colonic irrigation, wash out stomach, and leave 60 ml. of saturated magnesium sulphate in it. Then inject 1000 ml. of 20% dextrose solution during 30 to 50 minutes 2, 3 or 4 times daily. When stomach has emptied itself, inject 5% syrup water, beginning with 50 ml. and increasing hourly up to patient's tolerance, possibly up to 300 ml. an hour, until patient is conscious.—O. H. Schwarz, *J. Amer. med. Ass.*, ii/1929, 1679.

Of 201 cases treated, attacks were terminated in 136 after one injection; 69 patients went on to spontaneous delivery, while 132 were operated on; six died. The treatment was carried out as follows: The patient was placed in a darkened room and kept at absolute rest. Soon after an eclamptic fit or after admission, the patient was given from 0.015 to 0.02 g. of morphine hydrochloride and examination made under light chloroform anaesthesia. Thirty minutes later 40 ml. of a 15% solution of magnesium sulphate (6 g.) was given subcutaneously. Morphine was repeated one and a half hours later and magnesium sulphate 3½ hours later in a dose of 8 g., if there was another attack, or 4 g. when no further attack took place. If labour did not terminate, 4 g. of magnesium sulphate was injected at an interval of 6 and then of 8 hours later. If the fits did not cease, the full dose, i.e., 6 g., was given (but not to exceed 24 g. in 24 hours). Among the disadvantages of the drug are its toxicity, the tendency to development of abscesses at the site of injection, and a tendency to the development of psychoses (in some 2% of cases). In rare cases the injections of magnesium sulphate caused alarming symptoms, such as acute cyanosis, dyspnoea, and feeble pulse. Should this happen, 10 g. of a 5% solution of calcium chloride should be given intravenously.—W. Stroganoff and O. Davidovitch, *J. Obstet. Gynec.*, 1937, 44, 289.

**ENCEPHALOPATHY, HYPERTENSIVE.** Excellent results in children by slow intravenous injections of 10 to 15 ml. of 1% magnesium sulphate solution per kilo body weight, repeated at 12 to 24 hour intervals, and supplemented by giving the salt also by mouth or rectally. Alternatively, 40 ml. of a 30% sodium chloride solution intravenously.—Clifford Hoyle, *Practitioner*, ii/1933, 430.

**ERYSIPELAS.** A cold saturated aqueous solution of magnesium sulphate, containing 10 to 20% of glycerin, favoured.—W. T. Benson, *Lancet*, ii/1930, 1286.

**HEADACHE, e.g., post-concussional,** 4 to 8 oz. of 50% magnesium sulphate solution per rectum.—A. Feiling, *Brit. med. J.*, ii/1930, 907.

**MIGRAINE.** Of 74 cases, 45 obtained relief and 4 were cured by intravenous injections of a 50% solution of magnesium sulphate. A course of 12 injections was given, the first two of 2 ml., subsequently increased to 5 ml. The injection is given slowly with the patient lying down.—A. Schick, *Wien. klin. Wschr.*, 1937, 1205.

**OTORRHOEA.** Cleanse the meatus. Half fill the meatus with powdered magnesium sulphate (cryst.) and cover with a large piece of wool. Where discharge is free, four-hourly treatment is needed, otherwise once or twice a day suffices. As a rule the ear is dry in three weeks or less and hearing is greatly improved.—E. Watson-Williams, *Brit. med. J.*, ii/1933, 49.

**SYDENHAM'S CHOREA.** Intramuscular injections of a 25% aqueous solution most effective. In children of 1 to 5 an injection of 5 ml. is given deeply into the gluteal muscles every 2 days, and in older children 10 ml. In most cases improvement occurs after the second to the fifth injection, with cure after the tenth. Severe cases were often cured more rapidly than milder ones. No secondary effects and no renal or cardiac complications.—M. R. Coutreras, *Pr. méd.*, i/1936, 228.

**TETANUS.** Treatment of tetanus recommended by means of serum and subcutaneous injections of 40 ml. of 2.5% magnesium sulphate solution every four hours, the injections being continued for a varying period.—P. Paterson, per *Prescriber*, 1939, 305.

**TROPICAL ULCER** treated with wet dressings of magnesium sulphate 25% solution.—J. F. James, *Indian med. Gaz.*, June, 1925, 274.

**ULCERS** of the leg treated by soaks of 5 to 10% magnesium sulphate solution.—J. H. Young, *Lancet*, i/1925, 976.

**URÆMIA** successfully treated by slow intravenous infusion of a 1% solution (2 g.  $\text{MgSO}_4 \cdot 7\text{H}_2\text{O}$  in 100 ml. of distilled water). Indicated when blood pressure rises above 130 mm.—C. B. Watson, *Brit. med. J.*, ii/1931, 1086.

**Balneum Magnesii Sulphatis (B.P.C.).** Contains 1 lb. of magnesium sulphate per 30 gallons.

**Enema Magnesii Sulphatis (B.P.C.).** *Dose.*—20 ounces (600 ml.). 5% w/v in mucilage of starch with olive oil 10% v/v. A solution containing 50% w/v in hot water is also used, in doses of 2 to 6 oz.

**Liquor Magnesii Sulphatis (R.I. Edin.).** *Syn.* HENRY'S SOLUTION.

*Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.).

Magnesium sulphate  $\frac{1}{2}$  oz., dilute sulphuric acid 20 m., water to 1 oz. An occasional purge.

**Eau Saline Purgative (Fr. Cx.).** Magnesium sulphate 25, sodium sulphate 25, water to 650.

**Eau Saline Purgative Gazeuse (Fr. Cx.).** Magnesium sulphate 30, sodium bicarbonate 4, tartaric acid 4, water to 650.

**Magnesii Sulphas Effervescens (B.P.C.).** *Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 g.), or 1 to 3 drachms (4 to 12 g.) repeated.

Contains about 50% of magnesium sulphate which, in this form, is frequently more effective, and more palatable.

**Mistura Alba (B.P.C., N.I.F.).** *Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.).

Magnesium sulphate 120 gr. and light magnesium carbonate 20 gr. in peppermint water to 1 ounce. A mild aperient.

**BLOOD PRESSURE, TO REDUCE.** In uncomplicated hypertony give Mistura Alba as routine treatment. Drinking large quantities of water often beneficial.—I. Harris, *Lancet*, ii/1931, 1045.

[P1] **Mistura Salina Laxans (St. T. H.).** Magnesium sulphate 30 gr., potassium citrate 20 gr., tincture of hyoscyamus 15 m., chloroform water to 1 oz.

**Magnesii Sulphas Exsiccatus (B.P.C., P. Helv. V, P. Dan.).**

*Dose.*— $\frac{1}{2}$  to 3 drachms (2 to 12 g.).

Prepared by heating magnesium sulphate at 100° until it has lost 25% of its weight. A white powder *soluble* 1 in 2 of water. Contains 62 to 70% of  $\text{MgSO}_4$ .

**Pasta Magnesii Sulphatis (B.P.C.).** *Syn.* MORISON'S PASTE.

Prepared with magnesium sulphate dried to constant weight at 100°, when the loss in weight is about 37%, by mixing 4 $\frac{1}{2}$  parts with 5 $\frac{1}{2}$  parts, by weight, of glycerin and incorporating 0.5% of phenol.

Morison's original paste was prepared by mixing 1 $\frac{1}{2}$  lb. of exsiccated magnesium sulphate with 11 ounces of glycerin of phenol (the phenol may be omitted). The exsiccated magnesium sulphate used was "in the form of a fine white powder containing



12% less water than the ordinary."—(See A. E. Morison, *Brit. med. J.*, i/1924, 703; also *ibid.*, i/1918, 342.)

Was originally advocated for the treatment of wounds, later for boils and carbuncles. For wounds the dressing of gauze and wool is left unchanged for 6 to 8 days unless more wool is required, and after a few such dressings a magnesium sulphate solution is applied. The paste is applied to boils, carbuncles, etc., until a slough has separated.

**Pasta Mag. Sulph.** (*N.I.F.*). Exsiccated magnesium sulphate 432 gr., glycerin 528 gr.

**Magnesium Sulphate and Ethylene Glycol Paste.** Magnesium sulphate 60% and ethylene glycol 40% "by volume." Heat the ethylene glycol to boiling and slowly add the magnesium sulphate, stirring thoroughly until the solution becomes adherent to the stirring rod. Then mix in an electric mixer for 20 to 25 minutes. Allow to stand for 10 days before use, stirring daily for five minutes. The paste is changed every eight hours in severe cellulitis. Furuncles should be dressed repeatedly, but the application need not be covered.—J. W. Hinton, *Arch. Surg.*, ii/1936, 210.

## MALTUM

*Syn.* CEBADA GERMINADA (*F.E. VIII*).

Grain of barley, *Hordeum distichon* (Gramineæ), partially germinated artificially and then dried. The source of pharmaceutical, veterinary and baker's malt extract and of malt flours for bread making and infants' foods.

Malt flour or entire malt powdered, is added to baked wheaten flour in various proportions to form the popular infants' foods, and is given to assist digestion. When these are mixed with hot water or a mixture of hot milk and water, the starch contained in the wheaten flour becomes soluble and digested into dextrin and malt sugar. The diastasic property of malt is most active in aqueous solution at 104°F.—a boiling heat destroys it. A small teaspoonful of malt flour may be sprinkled over or mixed with cooked farinaceous foods, etc.

**Extractum Malti** (*B.P.*). *Syn.* EXTRACTUM BYNES, EXTRAIT D'ORGES. DIAMALT (*British Diamalt Co., London*), KEPLER (*Burroughs Wellcome, London*), and MALTINE (*Glaxo Laboratories, London*) are proprietary brands of extract of malt. (*Note.*—Maltine in France is a synonym for diastase.)

*Dose.*—1 to 4 drachms (4 to 16 ml.).

A brownish, semi-liquid substance, sp. gr. 1.40 to 1.42, with pleasant sweet taste, consisting principally of maltose (about 50%), with dextrin, dextrose, diastase, protein, phosphates and aromatic principles. The *B.P.* requires a nitrogen content equivalent to 4.5% *w/w* of protein. It is made by mixing malt with tepid water (55°), pressing, filtering, and evaporating *in vacuo* at below 55°. Extract of malt and its preparations are prescribed in cases of debility of all kinds, as a restorative, but particularly where digestion is weak. Commercially, malt extracts are assayed for their

diastasic power (Lintner value) but since diastase is inactive *per os* no such assay is required by the B.P.

**Maltosan** (*A. Wander, London*) is malt extract in granular form.

**Extractum Malti** (*U.S.P. XI*). *Average dose*.— $\frac{1}{2}$  oz. (15 g.).

It can convert not less than five times its weight of starch into water-soluble sugars, and unlike the product of the British Pharmacopœia its diastasic activity is regarded as the factor of primary importance.

*F.E. VIII* incorporates 10% of glycerin and the finished product must digest five times its weight of potato starch at 40°.

**Extractum Malti cum Oleo Morrhuæ** (*B.P.*).

*Dose*.—1 to 4 drachms (4 to 16 ml.).

Contains 10% *w/w* of cod-liver oil, equivalent to approximately 15% *v/v*.

**Extractum Malti cum Oleo Vitaminato** (*B.P. Add. II*).

*Dose*.—1 to 4 drachms (4 to 16 ml.), approximately equivalent to 650 to 2500 units of vitamin A, and 65 to 250 units of vitamin D.

Contains 10% *w/w* of vitaminised oil, equivalent to approximately 15% *v/v*. It is an efficient substitute for extract of malt with cod-liver oil.

**Ext. Malt. c. Ol. Hippoglossi** (*D.T.F.*). Halibut-liver oil 16 m., arachis oil 180 m., extract of malt to 1 lb.

**Extractum Malti cum Oleo Olivæ** (*B.P.C.*).

*Dose*.—1 to 2 drachms (4 to 8 ml.).

Olive oil 15% *v/v* in extract of malt.

**Extractum Malti Ferratum** (*B.P.C.*).

Soluble iron pyrophosphate  $\frac{1}{2}$  dissolves in water and mixed with extract of malt.

*Dose*.—1 to 4 drachms (4 to 16 ml.).

**Ext. Malt. c. Syr. Ferri Phos. Co.** (*D.T.F.*). Compound syrup of ferrous phosphate 25% *w/w* in extract of malt.

**Extractum Malti Liquidum** (*B.P.C.*).

*Dose*.—1 to 4 drachms (4 to 16 ml.).

In place of evaporating malt infusion to the viscosity of the soft extract, it is concentrated *in vacuo* until it has sp. gr. 1.375, and about 10% of alcohol added, making the finished product of sp. gr. about 1.23. It may also be prepared by diluting the soft extract (67 $\frac{1}{2}$ % *v/v*) with alcohol and water.

**Extractum Malti Liquidum cum Cascara.**

*Dose*.—1 to 4 drachms (4 to 16 ml.). Liquid extract of cascara 1, liquid extract of malt 7. This is palatable. Mix and mark "Shake."

**Extractum Malti Liquidum cum Glycerophosphatibus** (*B.P.C.*).

*Dose*.—1 to 4 drachms (4 to 16 ml.).

Contains 2 gr. each of sodium and potassium glycerophosphates in 4 dr.

**Extractum Malti Liquidum cum Hæmoglobino** (*B.P.C.*).

*Dose*.—1 to 4 drachms (4 to 16 ml.). Contains 30 gr. of hæmoglobin in 4 dr.

**Extractum Malti Liquidum cum Hypophosphitibus** (*B.P.C.*). *Dose*.—1 to 4 drachms (4 to 16 ml.).

Contains 1 gr. each of calcium and sodium hypophosphites in 4 dr.

**Extractum Malti Liquidum cum Pancreatina.** *Dose*.—1 to 4 drachms (4 to 16 ml.).

Liquid extract of malt 2, solution of pancreatin 1.

[P] **Extractum Malti Liquidum cum Quinina et Strychnina** (*B.P.C.*).

*Dose*.—1 to 4 drachms (4 to 16 ml.).

Contains quinine hydrochloride  $\frac{1}{2}$  gr. and strychnine hydrochloride  $\frac{1}{4}$  gr. in 4 dr.

**Extractum Malti cum Vitaminis (B.P.C.).**

*Dose.*— $\frac{1}{4}$  to 1 ounce (8 to 30 ml.)

Contains solution of vitamin A and solution of irradiated ergosterol and is about three times as potent as extract of malt and cod-liver oil. 1 dr. contains about 3000 units of vitamin A and 225 units of vitamin D.

**Extractum Malti Liquidum et Medullæ Rubræ (B.P.C.).**

*Dose.*—1 to 4 drachms (4 to 16 ml.).

Equal parts of liquid extract of malt and extract of red bone marrow.

**Mistura Ferri cum Malto (B.P.C.).**

*Dose.*—1 to 2 dr. (4 to 8 ml.).

Contains 3 gr. of soluble iron pyrophosphate per dr.

**Bronamalt** (*Fletcher, Fletcher & Co., London*). A combination of a hydrobromic extract of cinchona with a liquid malt. *Dose.*—1 to 2 drachms with or immediately after meals. In cases of impaired nutrition and loss of appetite, especially in children.

**Bynin** (*Allen & Hanburys, London*). A brand of liquid extract of malt. Also available in numerous combinations including liquid paraffin, glycerophosphates, hæmoglobin, liver extract, stomach extract, hypophosphites, lecithin, pancreatin and phosphates. [P1] Bynin Amara contains in 1 oz. quinine phosphate  $1\frac{1}{2}$  gr., iron phosphate 2 gr., strychnine phosphate  $\frac{1}{16}$  gr., in liquid extract of malt.

**Jecomalt** (*Wander, London*). A dry extract of malt with cod-liver oil, in yellow granular powder.

**Ostomalt** (*Glaxo Laboratories, London*). Standardised concentrated malt preparation of vitamins A, B complex, C and D, with calcium glycerophosphate.

**Radio-Malt** (*British Drug Houses, London*). A malt extract preparation containing vitamins A, B<sub>1</sub>, B<sub>2</sub> and D.

**Vimaltol** (*Wander, London*). A preparation of malt extract with vitamins A and D as a concentrate of cod-liver oil and vitamin C from orange juice.

**Diastasum (B.P.C., Fr. Cx., P. Jap. V). Syn. AMYLASE.**

*Dose.*—1 to 5 grains (0.06 to 0.3 g.).

An enzyme obtained from an infusion of malt, prepared at below 60°, by precipitation with alcohol. Occurs as a yellowish or whitish amorphous powder, almost entirely soluble in water. Converts starch into sugars and dextrin, and is used in amylaceous dyspepsia in conjunction with pepsin.

**Incompatible** with acids, alkalis, alum, iron salts and tannin.

**Taka-Diastase** (*Parke, Davis, London*). Amyolytic enzyme derived from species of *Eurotium oryzae* cultivated on wheat bran. *Dose.*—5 grains. For the treatment of amylaceous dyspepsia.

**Takazyma** (*Parke, Davis, London*). Powder containing magnesium carbonate, bismuth carbonate, Taka-Diastase, calcium carbonate and ginger. *Dose.*—1 to 2 teaspoonfuls in water. For hyperchlorhydria.

**Maltosum (B.P.C.).**  $C_{12}H_{22}O_{11}, H_2O = 360.2$ .

Consists of  $\beta$ -maltose obtained from starch by hydrolysis with diastase. Crystallises from water as the monohydrate, from alcohol as the anhydrous substance. Used in bacteriological culture media.

**Dextri-Maltose.** (*Mead, Johnson & Co., Evansville; Brooks & Warburton, London*). A powder containing 51% of maltose, 42% of dextrin and 5% of water and, at choice, salt free, or containing sodium chloride 2%, potassium bicarbonate 3%, or with vitamin B. No. 1 (with salt) is for infant feeding, No. 3 (with potassium bicarbonate) for infants who suffer from constipation.

No. 2 (salt free) for use by practitioners who prefer to make their own salt additions.

**Malto-Dextrin** (*Glaxo Laboratories, London*). A mixture of dextrins, malto-dextrins and maltose for modifying milk mixtures; it contains no unaltered starch. Composition approx. 50% of maltose and 50% of dextrin and malto-dextrin.

## MANGANUM

Mn = 54.93.

Traces of manganese occur naturally in all organs of man and animals. When administered by the mouth the salts of manganese (with the exception of the permanganates) produce no noticeable effect and they are little employed in this manner, except in conjunction with iron in the treatment of microcytic anæmia.

Chronic manganese poisoning, resulting from exposure to the dust produced in certain grinding processes, is an industrial hazard. The condition is not observed in the uses of manganese not involving the production of dust.

**POISONING.** Manganese poisoning has been added to the list of diseases acquired in a factory or workshop that must be notified by the practitioner attending a case. The signs and symptoms are a stolid mask-like face, a low monotonous voice, and cramp in the legs, with muscular twitchings and increased tendon reflexes, ankle and patellar clonus. The patient shows retropulsion and propulsion and has a peculiar "slapping" gait. There are also emotional disturbances and occasionally uncontrolled laughing or crying.—*Lancet*, ii/1936, 412.

A report of 4 cases of chronic manganese poisoning in men working in the same manganese works, the symptoms appearing in one case after only 8 months' work and in the other three after 2½, 6½, and 8 years respectively. Clinical picture indistinguishable from chronic post-encephalitic parkinsonism; signs and symptoms of hepatic cirrhosis not found.—D. Owen, *Brit. med. J.*, ii/1934, 833.

**Mangani Butyras.**  $(C_3H_7\cdot COO)_2Mn = 229.0$ .

**Dose.**—1 to 1.5 ml. of 1% solution intramuscularly—not more than 3 injections should be given with 3 or 4 days' clear interval between them.

A pale pink powder having only a slight odour of butyric acid. Is precipitated as a heavy oily liquid by interaction of solutions of sodium butyrate and manganese chloride. This oil is washed with water, dried over sulphuric acid, and then washed with ether to remove free butyric acid. The product is again dried over sulphuric acid for some days, and powdered.

**Soluble** 1 in about 6 of water. The substance is hydrolysed by boiling water with deposition of manganese hydroxide.

**Uses.** Boils, carbuncles and other staphylococcal skin infections have been treated by intramuscular injections of a 1% solution of manganese butyrate, injections of 1 to 2 ml. being given at intervals of five days, with a maximum of three injections. The addition of sodium thiosulphate ½ gr. to the solution has been stated to reduce the pain of the injection.

The therapeutic claims made for any or all of the manganese salts (including manganese butyrate) in the treatment of cutaneous diseases and coccigenic infections are unsubstantiated. The evidence as to their scientific value is inconclusive and inadequate, and they are unacceptable for inclusion in N.N.R.—*J. Amer. med. Ass.*, i/1940, 248.

**BOILS.** The most satisfactory treatment for boils, recurring or non-recurring, is intramuscular injections of manganese butyrate. Moist dressings are unnecessary.—H. L. McCormick, *Brit. med. J.*, ii/1932, 780. Value confirmed.—A. P. Bertwistle, *ibid.*, 904.

**MINERS' BOILS AND CARBUNCLES.** Manganese injections recommended.—S. W. Fisher, *Lancet*, i/1931, 750.

**Mangani Carbonas** (*Fr. Cx.*).  $\text{MnCO}_3 \cdot \text{H}_2\text{O} = 132.9$ .

A white powder with a faint pink tinge. Insoluble in water, but slightly soluble in the presence of carbon dioxide.

**Mangani Chloridum.**  $\text{MnCl}_2 \cdot 4\text{H}_2\text{O} = 197.9$ .

*Dose.*—5 grains (0.3 g.);  $\frac{1}{2}$  to  $\frac{1}{4}$  grain by injection (0.016 to 0.03 g.).

Rose coloured deliquescent crystals, soluble about 1 in 1 of water, and in alcohol 90%.

**DEMENTIA PRÆCOX** (but not cases with active organic disease) treated by 30 half-weekly injections intravenously of from 2 to 8 ml. of a 0.02% solution: then 0.3 g. manganese chloride *per os* twice daily for a month. Improves physical condition, but optimum intravenous dose should not be exceeded.—G. E. Reed, *per Med. Annu.*, 1931, 316.

**Mangani Citras**, "Soluble."

*Dose.*—3 to 5 grains (0.2 to 0.3 g.).

This, a double salt with sodium citrate, and Ferro-Mangani Phosphas—*dose.*—3 to 10 grains (0.2 to 0.6 g.)—are scale preparations.

**Mangani Hypophosphis.**  $\text{Mn}(\text{H}_2\text{PO}_3)_2 \cdot \text{H}_2\text{O} = 203.0$ .

*Dose.*—1 to 5 grains (0.06 to 0.3 g.).

A white or slightly rose-tinted powder, soluble 1 in 7 of water. A nerve stimulant.

**Mangani Dioxidum Præcipitatum** (*B.P.C.*). *Syn.* MANGANI PEROXIDUM PRÆCIPITATUM.  $\text{MnO}_2 = 86.93$ .

*Dose.*—2 to 8 grains (0.12 to 0.5 g.) or more, in pills with syrup. Tablets, 2 grains (0.12 g.).

A bulky blackish brown powder, free from grittiness and entirely soluble in cold hydrochloric acid. In gastrodynia, pyrosis, and in amenorrhœa taken 3 or 4 times a day before expected period. In microcytic anæmia it assists the action of iron salts, and is less irritant than the permanganates.

**Mangani Sulphas** (*Fr. Cx.*). *Syn.* SULFATO DE MANGANESO (*F.E. VIII*).  $\text{MnSO}_4 \cdot 4\text{H}_2\text{O} = 223.1$ . *Dose.*—2 to 10 grains (0.12 to 0.6 g.).

A white powder with a faint pink tint, due to a little manganic sulphate, or in pink crystals. Soluble about 1 in  $1\frac{1}{4}$  of water.

Given in conjunction with iron in anæmia.

**Potassii Permanganas** (*B.P., U.S.P. XI, Fr. Cx., etc.*).  $\text{KMnO}_4 = 158.0$ .

*Dose.*—1 to 3 grains (0.06 to 0.2 g.) in well-diluted solution, or in pill. *U.S.P. XI* average dose 1 grain.

In purple crystals with astringent taste, soluble about 1 in 20 of water.

**Incompatible** with all vegetable oxidisable matter, *e.g.*, glycerin, alcohol, sugar, fats and oils, with ammonia, ammonium salts and alkaloids.

**Antidotes.** Empty stomach by stomach tube. Give medicinal charcoal, stirred up in water. Keep patient lying down and warm. Strychnine,  $\frac{1}{4}$  gr., hypodermically. Calcium bromide intravenously or calcium gluconate intramuscularly has been recommended.

A fatal case of poisoning in a young man following injection into the urethra of a solution of 25 g. of the crystals in a teacupful of water. Other fatalities have been recorded following ingestion of 15 to 20 g. of the crystals.—S. G. Willimott and M. Freiman, *Brit. med. J.*, i/1936, 58.

The brown stain caused by solutions can be removed from the skin by oxalic or sulphurous acid.

**Uses.** Potassium permanganate possesses oxidising, deodorising and astringent properties. Although it is markedly bactericidal *in vitro* its clinical value as a bactericide is minimised by its rapid reduction in the presence of body fluids.

Because of its oxidising action it is a valuable cleansing agent for wounds and mucous membranes, especially in suppurating and fœtid conditions such as cancerous ulcers. In dilute solution, e.g., 1 in 10,000 to 1 in 2000, it is extensively employed for washing out internal cavities such as the vagina and bladder; in the former strength it is widely used as an irrigation in the treatment of gonorrhœa in the male, not less than a quart of warmed solution being introduced into the meatus, employing either a syringe or douche-can with nozzle. The application of a 1 in 1000 solution is stated to prevent the occurrence of venereal disease if employed immediately after exposure to infection. As a gargle or mouth-wash a 1 in 5000 solution is of value as an antiseptic deodorant, though its nauseous taste is a disadvantage. A 1% solution is also said to be useful in bromidrosis and in various types of mycotic infection such as athlete's foot. Poison ivy dermatitis is well treated by application of this solution, and potassium permanganate baths (5 to 6 g. to a bathful of water) have been employed in the treatment of smallpox, especially in confluent cases, to reduce the smell and sloughing.

The crystals are widely used as an antidote to snake-bite poisoning. The venom is squeezed out, the area round incised, and the crystals rubbed in. The action is purely a chemical one and the treatment is only effective if used immediately.

It is little used internally, since owing to its oxidising action on the gastric mucosa it is liable to produce vomiting, but it has been recommended in cholera, in 2 gr. doses, to destroy the bacterial toxins, and in the treatment of asylum dysentery a solution of 1 gr. in 20 ounces has been employed in a dose of  $\frac{1}{2}$  to 1 ounce several times a day. Potassium permanganate is reputed to have emmenagogue properties and it has been used for this purpose in the treatment of amenorrhœa in doses of 1 to 2 gr. three or four times daily, but it is of doubtful value and is not recommended.

**ANTIDOTAL ACTION** is distinct but limited: even fairly dilute solutions are irritant, and a large dose may cause death. Potassium permanganate may be given orally in concentrations varying from 1 : 5000 to 1 : 2000, and 1 : 5000 may be used for washing the stomach, in poisoning by aconitine, amidopyrine, morphine, phenazone, picROTOXIN, and strychnine. It will not destroy all the poison, and its use should be followed by evacuation of the stomach. It is useless as an antidote in poisoning by atropine, cocaine, phosphorus, and by most of the synthetic hypnotics. There is no justification for the intravenous, subcutaneous, or intramuscular injection of potassium permanganate for the destruction of any poison in the circulation.—R. A. Hatcher, *J. Amer. med. Ass.*, ii/1935, 502.

**TROPICAL ULCER.** Soak a pledget of cotton wool in a saturated (5%) solution of potassium permanganate and apply to the sloughing floor of the ulcer. Small sloughs seem to be burnt away by this and larger sloughs are removed with scissors. The "cauterising" process is continued in each part of the ulcer until the patient feels the burning. The ulcer is finally filled with 1 in 5 iodoform-boric dusting powder covered with absorbent wool and bandaged till the next day, when it will show a large granulating surface with a few patches of phagedena

and a fine layer of iodoform over the whole area. Cases needing more than two such treatments are rare.—K. W. Todd, *Brit. med. J.*, ii/1939, 688.

**Thyroid and Manganese Treatment.** Acute infections, joint diseases, heart disease, abnormal blood pressure, diseases of pregnancy, disorders of metabolism, digestive troubles, nerve complaints, pulmonary diseases, diseases of the skin, goitre and myxoedema, disease of the breast, etc., treated by rectal injections of potassium permanganate 1 gr. in  $1\frac{1}{2}$  pints of sterile warm water. The amount is varied according to case, e.g., 2 doses of  $\frac{1}{2}$  pint may be found more effective than 1 dose of  $\frac{1}{2}$  pint. Warm patients they may feel some pain in the epigastrium within a few minutes, also they may pass long white skins or strings of mucus in the stools. Thyroid is given simultaneously—1 gr. twice daily, but doses of  $6\frac{1}{2}$  gr. or 5 or 10 gr. are in some cases desirable. Sometimes the permanganate may be used *per os*, in cachet, followed by a large draught of water, but this is not so good.—H. W. Nott, *Brit. med. J.*, i/1925, 443; ii/1925, 1209.

**PNEUMONIA.** Remarkable results. It is suggested that permanganate may be a specific. Treatment consists in rectal injections of 3 to 10 ounces of a potassium permanganate solution (4 grains in 3 pints) every 2 or 4 hours.—H. W. Nott, *Brit. med. J.*, ii/1926, 109. Basic principles underlying the treatment.—H. W. Nott, *Brit. med. J.*, i/1928, 94. See also *Brit. med. J. Epit.*, ii/1929, 43.

Value of treatment confirmed in 5 consecutive cases of acute pneumonia.—N. J. Roche, *Brit. med. J.*, i/1927, 459. See also *Brit. med. J.*, i/1927, 539.

A 1 in 7000 solution per rectum 4-hourly of value, even in debilitated children almost moribund; in conjunction with antipneumococcus vaccine a good armamentarium.—A. A. Hearne, *Brit. med. J.*, i/1928, 159. H. L. McCormick, *ibid.*, 377.

**Manganese and Thyroid.** "The most sure, the most scientific, the easiest treatment of all forms of cold or influenza."—F. A. Hort, *Brit. med. J.*, i/1933, 250.

**Gargarisma Potassii Permanganatis (B.P.C.).** 0.025% w/v.

**Injectio Potassii Permanganatis (L.H.)** has 5 grains in 1 pint, i.e. about 1 in 1600. C.H.W. has 1 in 1000 solution 4 dr., water to 2 pints, i.e. about 1 in 80,000.

**Liquor Potassii Permanganatis (B.P.C.).** Dose.—2 to 4 drachms (8 to 15 ml.). 1% w/v.

**Pilula Potassii Permanganatis.** 1, 2, 3, 4 or 5 grains with kaolin ointment, q.s.

**Caution!** Avoid mixing with any easily oxidised substance, like sugar, glycerin, etc. The pills may be coated with sandarac solution.

**Solvella Potassii Permanganatis** contain 5 gr. (0.3 g.).

**Calcii Permanganas (B.P.C.).**  $\text{Ca}(\text{MnO}_4)_2 \cdot 5\text{H}_2\text{O} = 368.0$ .

**Dose.**— $\frac{1}{2}$  to  $1\frac{1}{2}$  grains (0.03 to 0.1 g.) in pills or capsules (with liquid paraffin as vehicle) thrice daily one hour before meals.

Deliquescent crimson crystals preferred for making mouth lotions, as it has less taste than the potassium salt. 1 in 100,000 sterilises water in 5 minutes; more powerful than the latter.

**Uses.** Similar to the potassium salt. Has been given in gastric ulcer and gastritis, and employed as a local application in rodent ulcer.

**Sodii Permanganas.**  $\text{Na}_2\text{Mn}_2\text{O}_8 = 283.9$ .

In solution, red in colour, is used as a cheap disinfectant. **Condy's Red Fluid** (Condy & Mitchell, London; Pharmaceutical Products, London) is stated to be a mixture of the sulphate and permanganate of soda.—H. R. Kenwood, *Lancet*, i/1926, 1055. **Condy's Green Fluid** has sodium manganate,  $\text{Na}_2\text{MnO}_4 = 164.9$ , in solution.

**Zinci Permanganas (B.P.C.).**  $\text{ZnMn}_2\text{O}_8 \cdot 6\text{H}_2\text{O} = 411.3$ .

Brownish-black deliquescent crystals soluble 1 in 3 of water (usually leaving some residue).

It possesses the oxidising properties of the potassium salt but

is more astringent. It is more readily reduced than the potassium compound. For lotions and injections, especially in urethritis, 1 gr. in 8 oz. (1 in 4000), where the astringent action of the zinc is indicated. As an eye wash 1 in 2000 to 1 in 1000. For pyorrhœa alveolaris and oral sepsis it is very useful as a mouth wash.

**Caution.** Is liable to explode spontaneously and if the stopper of a bottle containing it becomes stuck, the bottle should be wrapped in a cloth before removal is attempted.

**Zinc permanganate bougies**, 4 inches long, containing  $\frac{1}{2}$  grain (0.03 g.) in oil of theobroma basis, are prepared.

**Inject. Zinc. Permang.** (N.I.F.). Zinc permanganate 4 gr., water to 12 oz. To be diluted with an equal quantity of hot water (1 in 2625 when diluted).

**Colloidal Manganese.** A colloidal solution of manganese hydroxide may be prepared by double decomposition of manganese chloride and sodium hydroxide, using dextrose as protective.

**Uses.** Gonorrhœa and sequelæ, also eczema, acne, psoriasis, quinsy and furunculosis have been treated by it, either *per os* or by intramuscular injections of  $\frac{1}{2}$  to 1 ml.

In a carefully observed group of 43 patients with pustular acne, acne vulgaris, furunculosis, rosacea, and syphilis vulgaris, and also in a group of 9 patients with psoriasis, the results of treatment with a well-known brand of colloidal manganese hydroxide were unsatisfactory. There is no sound experimental basis for the claims made in respect of manganese and its compounds in the treatment of dermatoses.—M. Sullivan, *J. Amer. med. Ass.*, i/1940, 246.

## MENTHOL

B.P., U.S.P. XI, Fr. Cx., P. Jap. V, P. Helv. V, P. Dan.

$\text{CH}_3\cdot\text{C}_6\text{H}_4(\text{OH})\text{C}_3\text{H}_7 = 156.16.$

**Syn.** *l-p*-MENTHAN-3-OL, METHYL-PROPYL-PHENOLHEXAHYDRIDE.

**Dose.**— $\frac{1}{2}$  to 2 grains (0.03 to 0.12 g.), or more, in a pill with powdered soap, or in solution in olive oil.

A white crystalline substance obtained from the volatile oils of various species of *Mentha*. B.P. Add. I and U.S.P. XI recognise also levorotatory synthetic menthol. M.p. 42° to 44°.

**Soluble** 5 in 1 of alcohol 90%, 2 in 1 of ether, approximately 4 in 1 of chloroform, 1 in 4 of olive oil, 10 in 7 of light petroleum, and 1 in 6 of liquid paraffin. Freely soluble in essential oils, sparingly soluble in water, insoluble in glycerin. Soluble on warming in a strong solution of sodium salicylate, but thrown out again.

**Caution.** It is dangerous to apply an ointment containing menthol to the nostrils of infants, e.g., for treatment of catarrh—it may cause instant collapse. Cf. Camphor.

**Uses.** Given internally, it is carminative and is occasionally given in vomiting but is liable to upset digestion. Applied to the skin, it dilates the vessels, causing a sensation of coldness, and is useful for headache, rheumatic pains and neuralgia. For these purposes menthol cones are employed. It has antiseptic and anæsthetic properties, and gives great relief in prurigo, urticaria



and pruritus ani. An excellent mixture for pruritus ani consists of menthol 1 part, eucalyptol 2 parts, sodium baborate, sodium bicarbonate and powdered alum, each 8 parts.

As an antineuralgic in toothache and for sciatica 1 in 60 of alcohol with a little clove oil is employed as an external application. The crystals on cotton wool may be placed in the hollow of an aching tooth.

Menthol liquefies with an equal amount of either phenol, chloral hydrate or thymol, also 3 parts of menthol and 2 parts of camphor, 2 parts of menthol and 1 part of butylchloral hydrate, and 2 parts of menthol, with 1 each of phenol and butylchloral hydrate. These will relieve toothache. Its camphor and phenol combinations are used to medicate dry inhalers, and are most beneficial for arresting and curing colds, and relieving influenza and chest affections. Preparations of menthol are valuable for medicating hot moist air inhalations.

Menthol, camphor and other combinations, diluted with a heavy mineral oil, for spraying into the nares or in spirituous solution, inhaled as above, relieve swelling and irritability of nasal catarrh, contract capillary blood-vessels of mucous membrane, reduce swelling, relieve pain and fullness of head, arrest sneezing, and check excessive discharge.

**INFLUENZA.** In doses of  $7\frac{1}{2}$  grains, dissolved in olive oil in gelatin capsules, every 2 hours of value early in influenza. Reduces temperature in 18 to 24 hours, relieves pain, prevents post-influenzal debility, and lessens incidence of complications.—F. Schnapek, per *Brit. med. J. Epit.*, ii/1933, 61.

**TUBERCULOUS LARYNGITIS.** In the simpler non-ulcerative forms, 5 to 10% menthol in olive oil dropped on to the cords during phonation from a laryngeal syringe gives appreciable relief, the menthol acting as a decongestive and anæsthetic.—R. C. Cohen, *Brit. med. J.*, i/1940, 322.

### **Aqua Mentholis (B.P.C.).**

**Dose.**— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.). A saturated aqueous solution (about 1 in 1000).

**Emplastrum Mentholis (B.P.C.).** 15% in a basis of yellow wax and colophony. Useful for rheumatism and intercostal neuralgia.

### **Injectio Mentholis.**

Menthol 0.5, liquid paraffin 100. For use with a eustachian catheter to the middle ear.

**Insufflatio Mentholis (B.P.C.).** *Syn.* INSUFFLATIO MENTHOLIS COMPOSITA, MENTHOL SNUFF. Menthol 5% in ammonium chloride, boric acid and lycopodium. Relieves nasal catarrh.

[D·P1·S1] **Insufflatio Mentholis et Cocainæ (B.P.C.).** Menthol  $2\frac{1}{2}\%$ , and cocaine hydrochloride 0.14% ( $\frac{1}{8}$  gr. per oz.) with ammonium chloride, camphor and lycopodium.

### **[P1] Linimentum Mentholis.**

Menthol 3, chloroform 4, olive oil q.s. to 16. Useful in lumbago, neuralgia, sciatica, and ringworm.

[P2] **Menthophenol.** Menthol 3, phenol 1. Useful as gargle; 15 drops to the tumbler of water.

**Nebula Mentholis.** 0.5 to 2% in light liquid paraffin or olive oil is used for spray or pigment for throat. Relieves acute laryngitis.

**Nebula Mentholis Composita.** Menthol and camphor, 20 gr. each, cinnamon oil 5 m., light liquid paraffin to 1 oz.

**Nebula Mentholis et Thymolis Composita (B.P.C.).** Menthol, camphor and phenol, of each 2% *w/v*, with thymol, in light liquid paraffin.

**Narist. Menthol. et Thymol. (N.I.F.).** Menthol 2 gr., thymol 1 gr., eucalyptol 1 m., liquid paraffin to 1 oz.

[P1] **Neb. Menthol. c. Benzamin. (N.I.F.).** Menthol 10 gr., benzamine 5 gr., oleic acid 10 m., light liquid paraffin to 1 oz.

**Pastilli Mentholis (B.P.C.)** contain  $\frac{1}{10}$  gr. (0.003 g.).

[P1] **Pastilli Mentholis et Cocainæ (B.P.C.)** contain menthol  $\frac{1}{10}$  gr. and cocaine hydrochloride  $\frac{1}{10}$  gr.

**Pigmentum Mentholis.** Menthol 1, olive oil 4. Painted or injected into the larynx, or even the trachea, is useful in phthisis and laryngeal disease. Also applied on wool for ear affections.

A solution of menthol 60 gr. in liquid paraffin or olive oil to 1 oz. is known in some clinics as "Pigmentum Melbæ," and is a great favourite with professional singers.—D. McKenzie, *Practitioner*, ii/1935, 663.

**Pigmentum Mentholis cum Guaiacol.** Menthol 1 gr., guaiacol in crystals 1 gr., oil of almond to 1 oz. Is often of value in acute tonsillitis.

**Pigmentum Mentholis et Tolueni (B.P.C.).** *Syn.* LÖFFLER'S PAINT. Menthol 10% *w/v*, with dehydrated alcohol, strong solution of ferric chloride and toluene. For diphtheria; to be applied on wadding every 3 hours. Painful in use; dilute hydrogen peroxide is preferable.

**Pilula Mentholis.**  $\frac{1}{2}$  to 2 grains. Mass with powdered soap or half its weight of white wax previously just melted.

[D-P1-81] **Pulvis Mentholis et Cocainæ Compositus.** *Syn.* POUDRE CONTRE LE CORYZA (*Fr. Cx.*).

Menthol 1, cocaine hydrochloride 0.5, bismuth salicylate 45, boric acid 53.5.

**Spiritus Mentholis (B.P.C.).** 1 in 20.

**Spiritus Mentholis Compositus (B.P.C.).**

*Dose.*—10 drops, by inhalation. Camphor, menthol, terebene and eucalyptol, of each 1 in 10, in alcohol 90%.

[P1] **Tinctura Mentholis Ætheræa.**

Menthol 1, ether 4 and chloroform 4. For local application in neuralgia.

**Unguentum Mentholis et Camphoræ.** Menthol 3% and camphor 2% in white soft paraffin. To be applied to the nasal passages in small quantity for hay fever.

**Ung. Menthol. et Eucalypt. (N.I.F.).** Menthol 5 gr., oil of eucalyptus 20 m., white soft paraffin to 480 gr.

**Vapor Mentholis Citriodoratus.**

Menthol, oil of *Eucalyptus Citriodora*, Cologne spirit and alcohol 90%, of each, equal parts. A little inhaled, *e.g.*, from an oro-nasal inhaler or the handkerchief, is valuable for nasal catarrh and influenza.

**Vapor. Menthol. et Eucalypt. (N.I.F.).** Menthol 20 gr., oil of eucalyptus 2 dr., liquid paraffin to 1 oz.

**Menthylis Valerianas.**

*Dose.*—10 to 15 minims (0.6 to 1 ml.).

A colourless liquid with agreeable odour and free from the burning taste of menthol. Nerve sedative. Used in sea-sickness.

*Validol (Boehringer, Mannheim; Coates & Cooper, London)* is a mixture of menthol and menthyl valerianate. Available as liquid or in perles.

## MORPHINA

B.P.C., Fr. Cx., F.E. VIII.



[D] "*Morphine and its salts, the esters of morphine and their respective salts.*"

"*Any solution or dilution of morphine or its salts in an inert substance, whether liquid or solid, containing any proportion of morphine, and any preparation, admixture, extract or other substance (not being such a solution or dilution as aforesaid) containing not less than one-fifth per cent. of morphine.*"

"*All preparations of esters of morphine.*"

[P1] "*Alkaloids, the following; their salts, simple or complex:—Morphine.*"

[S1] "*Alkaloids, the following; their salts, simple or complex:—Morphine except substances containing less than 0.2% of morphine calculated as anhydrous morphine.*"

NOTE.—*The esters do not include and should not be confused with the ethers of morphine, e.g., methyl-morphine (codeine) and ethyl-morphine (dionin).*

Dose.— $\frac{1}{8}$  to  $\frac{1}{2}$  grain (0.008 to 0.02 g.).

MORPHINE FOR CHILDREN. The dose of morphine for children (in pre-operative medication) is often estimated in a haphazard fashion; it should be calculated according to body weight. If  $\frac{1}{8}$  gr. is taken as the standard dose for a 10-stone man a child of 1 stone should be given gr.  $\frac{1}{8} \times \frac{10}{10} = \frac{1}{8}$  gr., whilst a child of 7 lb. would receive  $\frac{1}{8} \times \frac{7}{10}$  gr.—R. R. Macintosh, *Practitioner*, ii/1939, 544.

This, the principal alkaloid of opium, occurs as a white powder, or white, shining crystals. 3 parts of morphine are reckoned approximately equal to 4 parts of the acetate, hydrochloride or sulphate.

**Soluble** about 1 in 5000 of water, 1 in 100 of alcohol 90%, 1 in 4000 of chloroform, 1 in 3250 of benzene, 1 in 16 of aniline, 1 in 6 of pyridine; almost insoluble in ether. 1 in 125 of glycerin, 1 in 10 of oleic acid; solutions of its salts are precipitated by ammonia and by potassium hydroxide (but redissolve in the latter).

Solubility at 20° is 1 in 6700 of water, 1 in 410 of alcohol 60%, 1 in 300 of alcohol 90%, 1 in 38 of dehydrated alcohol, 1 in 900 of alcohol-free pure chloroform or 1 in 500 of commercial chloroform containing alcohol.—H. Baggesgaard-Rasmussen and F. Reimers, *Dansk Tidsskr. Farm.*, 1931, 5, 145.

**Incompatibility.** Morphine salts are decomposed by alkalis, and solutions are precipitated by vegetable compounds containing tannin. Also incompatible with iron, lead, manganese, silver, copper, and zinc salts and potassium permanganate.

The alkalinity of glass bottles may throw out a very appreciable amount of morphine from a solution of a salt.

**Antidotes.** Emetics probably not act, so empty stomach by stomach tube, using 60 gr. of potassium permanganate in 2 gallons of water and repeating the lavage frequently for a period

of some hours. Stomach washing should be carried out even if the morphine has been taken hypodermically, because it seems to be excreted partly into the stomach. Keep the patient warm; rouse him by constant attention, flap him with a wet towel but do not walk him about. Give hot black coffee by mouth and by rectum, and medicinal charcoal, stirred up in water, freely. Atropine is the physiological antidote, and may be given hypodermically,  $\frac{1}{100}$  gr., or as tincture of belladonna. Strychnine,  $\frac{1}{2}$  gr., or caffeine sodium benzoate, 2 gr., hypodermically; nikethamide, 5 to 15 ml. of 25% solution, intravenously. Artificial respiration and inhalations of oxygen with 7% carbon dioxide may be necessary. Urine must be drawn off with a catheter frequently.

(According to Sollmann, atropine, although the physiological antidote, may in some circumstances actually be a dangerous remedy, since the effects of morphine and atropine on circulation, respiration and metabolism are antagonistic only with certain stages; in the more severe grades of poisoning they are actually synergistic. Atropine is only useful therefore if given in moderate doses, i.e., not exceeding  $\frac{1}{10}$  gr., in moderate morphine poisoning.)

*Morphine poisoning* in a baby of 10 days (due to pre-anæsthetic injection of  $\frac{1}{8}$  gr. morphine) combated by a mixture of 10% carbon dioxide and 90% oxygen. This mixture is known in the U.S.A. as 10-90.—J. R. McCurdy, *J. Amer. med. Ass.*, i/1929, 1927.

**Treatment of Drug Addiction.** Morphine addicts are defined as persons who, not requiring the continued use of a drug for relief of symptoms of organic disease, have acquired, as a result of repeated administration, an overpowering desire for its continuance, and in whom withdrawal of the drug leads to definite symptoms of mental or physical distress or disorder. The withdrawal symptoms vary in intensity with the individual, the degree of addiction, and the rapidity with which the drug is withdrawn. They begin within 24 hours, become severe within 48 hours, reach their acme within 72 hours, and then gradually subside. They include violent pains and muscular twitchings, headache, weakness, insomnia, irritability, severe digestive disturbances, nausea, vomiting, loss of weight, diarrhoea, and vasomotor disturbances.

Withdrawal of the drug may be effected rapidly or gradually. The latter method, which is safer and causes less pain, and which requires from three to six weeks, is the method of choice in most cases. Whichever method is employed institutional treatment is essential, and the patient must be kept under continual surveillance.

The following are brief summaries of some of the more widely used methods:—

**Gradual Reduction Treatment** lasts about two months:—

*During the first 20 days* the amount of morphine hypodermically is decreased gradually, and the decrease made up either by giving the deficit, plus 25%, by the mouth, or by exactly replacing the amount of morphine stopped with codeine sulphate. A gradually increasing dose of strychnine, either with the injection or *per os*, should be given.

*The next 6 to 12 days* should see the codeine entirely replace the morphine hypodermically, the strychnine as previously should be given and the morphine

*per os* should be gradually diminished, though, of course, the volumes of all solutions given must remain the same. The daily amount of codeine must now be lessened, a period of about 10 to 20 days being occupied (according to the honesty and disposition of the patient) in reducing the amount to zero. During these last stages a bitter tonic should be given and a daily dose of hyoscyne hydrobromide of  $\frac{1}{4}$  gr. is required.

Acidosis should be treated with magnesia, and cascara is useful for the frequently attendant constipation.

**The Lambert-Towns Rapid Withdrawal Method** is one in which enormous quantities of blue pill are given, together with decreasing amounts of morphine and increasing quantities of belladonna, xanthoxylum and hyoscyamus mixture (*vide infra*). The treatment appears to culminate in the administration of 2 ounces of castor oil, the nervousness of the patient being controlled with codeine.

**The Pettey Method** (George E. Pettey) includes the administration of hyoscyne in  $\frac{1}{16}$  gr. doses, sparteine sulphate in 2 gr. doses and sodium thio-sulphate in doses of 20 gr. every 2 hours for 24 hours. Cathartic capsules containing calomel, cascara, ipecacuanha, strychnine and atropine are also given.

In these more rapid methods ethylmorphine is stated to be more efficacious than codeine; as it is about twice as powerful it is argued that half the dosage will suffice. This is taken advantage of in the following—

**Sceleth's Method**, in which ethylmorphine  $\frac{1}{4}$  gr. is combined with hyoscyne, pilocarpine and cascara, and an amount varying with the amount of morphine taken is administered daily for 10 days. Then strychnine  $\frac{1}{16}$  gr., 3 times a day for 1 day, and on the following day the dose is halved and continued for a week. In about 4% of the cases hyoscyne delirium has been observed. In such cases it should be omitted for a few doses.

Hyoscyne and pilocarpine constitute the bases of **Bishop's Method** with sometimes the addition of heroin during the active stage.

Gradual and cautious withdrawal covered by two successive waves of overdose by "Special Mixture" (consisting of equal parts of tincture of belladonna and the fluid extracts of hyoscyamus and xanthoxylum, and Luminal respectively). When the total dose is reduced to  $\frac{1}{4}$  grain in 24 hours, without discomfort, for two days saline is given in place of the drug. No distress at any stage and no crisis. Treatment lasts ten to fourteen days.—G. Laughton Scott, *Practitioner*, 1/1927, 56.

A 0.1% solution of quinine hydrochloride gives the same bitter taste as a 0.5% solution of morphine, and may be substituted for it without the patient's knowledge.—H. Alpers, *Münch. med. Wschr.*, 1935, 1327.

**Intensive Treatments of Morphine Addiction.** Rapid relief from the craving for the drug in a simplified, painless and non-hazardous manner without the usual discomfort of withdrawal. The patient is first assured that permanent relief from the habit is possible, and that he will receive absolutely no more morphine when the treatment is started. Owing to the increased psychomotor activity during the intensive phase of the treatment, constant nursing service is required. Saline catharsis 5 drachms (19 g.) of Karlsbad salt for one or two doses precedes treatment. Scopolamine and pilocarpine are given hypodermically as follows:—(1) Scopolamine hydrobromide  $\frac{1}{160}$  gr., 1 dose; (2) scopolamine hydrobromide  $\frac{1}{160}$  gr., 5 doses, 1 every hour; (3) scopolamine hydrobromide  $\frac{1}{160}$  gr., 21 doses, every 2 hours; (4) pilocarpine nitrate  $\frac{1}{4}$  gr. 2 hours after the last dose of scopolamine and continued for a total of 5 doses, 1 every hour. Every patient treated has stated that he did not recall what had taken place during the treatment, had not experienced any physical or mental distress whatever, and had no desire for morphine. After the intensive treatment (48 hours) the following powder is given and continued for 6 to 8 weeks to restore the blood calcium level, which falls during the administration of sedatives and hypnotic drugs:—Scopolamine hydrobromide  $\frac{1}{4}$  gr., calcium phosphate compound (magnesium phosphate 2, dibasic calcium phosphate 8, calcium glycerophosphate 8, potassium bicarbonate 32, sodium bicarbonate to 100) 2 drachms, divided into 24 doses, 1 capsule being taken 3 times a day before meals. Of 57 patients treated 55% were permanently relieved and 12% relapsed.—T. Klingmann and W. H. Everts, *J. Amer. med. Ass.*, 1/1936, 18.

The opium is suddenly withdrawn (with the patient's consent) and a dose of 1 to 3 gr. of calomel given at bedtime followed by a dose of salts next morning.

The salts are repeated every morning for the next few days to eliminate opium from the system and to stimulate liver function. On the day of withdrawal, or as soon as symptoms appear, lecithin is given by mouth in doses of 15 to 20 gr. thrice daily in form of pills (or by intramuscular injection, 2 ml. of 1% solution twice daily). The lecithin is continued till most of the major symptoms completely disappear (in 2 to 4 days). Plenty of fluids and dextrose are given by the mouth, and 25 ml. of 25% dextrose with 10 ml. of 10% calcium gluconate is given intravenously during the first five days of the treatment. The duration of the treatment varies from 7 to 12 days. This treatment has been employed with success on several thousand opium addicts who were taking doses of opium ranging from 45 to 250 gr. daily in Assam.—R. N. Chopra and G. S. Chopra, *Indian J. med. Res.*, 1940, 28, 225. See also *ibid.*, *Indian med. Gaz.*, 1937, 265; and R. N. Chopra and S. C. Gonguly, *Indian J. med. Res.*, 1939, 26, 699.

**Auto-serotherapy.** Blistering the patient and reinjecting the blister fluid, from two to five injections being given. The patient no longer needs or desires the drug. Remarkably good results in Egypt.—M. Vivian, *Lancet*, ii/1934, 273.

Successfully used in every one of eight cases. In obtaining the fluid, two, or even three or four, small blisters—e.g., 1½ inch square—are preferable to one large one, because they heal more easily. The fluid is withdrawn before the plaster is removed and is reinjected immediately, the amount injected being from 5 to 10 ml. hypodermically; it causes no pain or reaction of any kind. The treatment obviates the usual distressing withdrawal symptoms and removes the physical need for the drug within two or three weeks.—M. Vivian, *Lancet*, i/1937, 1221.

**THE TREATMENT OF DRUG ADDICTION:** an exhaustive review of modern withdrawal methods—"abrupt," "rapid," and "gradual"—with a bibliography of 57 references.—E. W. Adams, *Practitioner*, ii/1932, 234, 390.

**Contraindications.** Morphine and opium are contraindicated in children under one year of age, and in respiratory depression, especially in the presence of cyanosis and excessive bronchial secretion, also in asthenic bronchitis and after operations on the biliary tract. In the presence of marked hepatic deficiency only small doses should be given.

**Uses.** The chief uses of morphine, in the order of their importance, are the relief of pain, the procuring of sleep, the arrest of hæmorrhage, the checking of peristalsis, the suppression of cough, the relief of dyspnoea, and the quietening of muscular spasm. Morphine is the most valuable of all analgesics especially for persistent pain, though it is apt to give rise to indigestion and constipation.

It is invaluable in the treatment of shock, for relieving the pain (if present) and allaying the anxiety and restlessness; it may be given in a dose of ½ gr. either by the mouth, or by subcutaneous, intramuscular or intravenous injection. A second dose should not be given until at least four hours later; excessive dosage may increase the symptoms of shock.

In addition to its use in pathological conditions it is of value as a sedative for the relief of pain during the first stage of labour, but it should not be used in the later stages. Morphine is invaluable for the relief of insomnia due to pain, but it should be avoided if possible in nervous insomnia and in excitable conditions. As a pre-operative sedative it has now been largely replaced by the basal narcotics.

Morphine favours the arrest of hæmorrhage by soothing the patient, thus keeping the blood pressure low and permitting the formation of the clot; hypodermic injections of ½ gr. are especially

valuable in internal hæmorrhage, as from gastric or duodenal ulcer or the less severe forms of hæmoptysis. Shock due to hæmorrhage is also well treated by morphine.

Owing to its anti-peristaltic action, morphine is very effective in the treatment of diarrhœa and for the relief of pain in biliary and renal colic and the colic of lead poisoning; in peritonitis it is invaluable for alleviating the pain, but should not be given until a diagnosis has been made.

Its depressant action on the respiratory centre renders it valuable in the suppression of cough, especially of the irritative type, but its use is contraindicated where there is much expectoration, and if employed in phthisical cough it should be employed with expectorants. Injections of  $\frac{1}{4}$  gr. are useful in acute asthma and dyspnœa and for the relief of the respiratory distress and pain in acute respiratory diseases such as pneumonia and pleurisy.

Although morphine cannot compare with the anti-convulsants in the treatment of conditions such as tetanus, injections of  $\frac{1}{4}$  to  $\frac{1}{2}$  gr. are of undoubted value in the suppression of the convulsions of eclampsia.

Morphine acts only on certain pain centres in the brain, and is therefore wasted in lead and opium lotion and laudanum fomentations. Rectal morphine suppositories are efficacious only so far as morphine is absorbed and carried to the brain. We are apt to fear the secondary effects of morphine too much, rather than too little, and to forget that large doses of the synthetic products may cause sweating, rashes, and sometimes cyanosis.—E. B. Leech, *Lancet*, i/1924, 915.

May be given without fear of renal complications secondary to its use.—R. S. Ackley, *J. Amer. med. Ass.*, i/1930, 79; *Lancet*, i/1930, 364.

**MORPHINE AS A PRE-ANÆSTHETIC.** Morphine sulphate intravenously is used extensively at the Mayo Clinic as an adjunct to regional anæsthesia and in peroral endoscopy. The method may also be used in any case in which rapid action is desired, e.g., as a pre-anæsthetic medication, in emergencies. The amount used has varied from  $\frac{1}{8}$  to  $\frac{1}{4}$  gr. After about  $\frac{1}{8}$  gr. has been injected a pause of thirty seconds allows one to judge the response and to note possible idiosyncrasy. The injection is then slowly continued until the desired result is obtained. The advantages of the intravenous route are that full effect is at once attained, while the dose may be accurately controlled. The duration of effect is about the same as with hypodermic injection.—C. J. Betlach, *Proc. Mayo Clin.*, 1937, 733.

When average doses of Pentothal sodium given intravenously do not produce adequate anæsthesia, morphine sulphate in suitable doses may be injected through the same needle; subsequent doses of Pentothal sodium will usually result in adequate anæsthesia without use of excessive amounts of the drug. When local anæsthesia, particularly cervical block anæsthesia, is used for an extensive operation, morphine sulphate intravenously produces rapid sedation and relieves the patient of much discomfort so that the operation may frequently be completed without administration of a supplementary anæsthetic agent. It is also of value as an adjuvant to spinal anæsthesia, if towards the end of the operation the patient is beginning to experience some discomfort; also for tranquilising the patient prior to an operation under local or regional anæsthesia or before such procedures as œsophagoscopy or bronchoscopy. A sufficiently dilute solution of morphine should be used for intravenous administration so that a very small initial dose may be given—in this way any untoward effects may be noted and an overdose prevented; administration should be discontinued as soon as the patient feels the first effects, regardless of the amount of the dose. This may vary between  $\frac{1}{8}$  and  $\frac{1}{4}$  gr. (this latter amount should be diluted so as to make a total volume of 2 to 3 ml.).—J. S. Lundy *et al.*, *Proc. Mayo Clin.* 1939, 278.

**[D-P1-S1] Oleatum Morphinae.** Morphine 1, oleic acid 60. Dissolve.

Oleic acid will dissolve as much as one-tenth of its weight of pure morphine. Morphine is added to oleate of mercury to relieve pain.

**[D-P1-81] Morphinae Acetas (B.P.C.).**

$C_{17}H_{19}O_2N, C_2H_4O_2, 3H_2O = 399.2$ .

*Dose.*— $\frac{1}{2}$  to  $\frac{1}{2}$  grain (0.008 to 0.02 g.), which may be increased.

A white powder with faintly acetous odour. Soluble 1 in  $2\frac{1}{2}$  of water, about 1 in 100 of alcohol 90%, and 1 in 5 of glycerin.

**[P1] Linctus Morphinae Hydrocyanicus (Ogle's Drops) (St. G. H.).**

Dilute hydrocyanic acid 1 m., solution of morphine acetate 3 m., oxymel of squill to 1 dr.

**[D-P1-81] Liquor Morphinae Acetatis (B.P.C.).**

*Dose.*—5 to 30 minims (0.3 to 2 ml.). 1%.

**[D-P1-81] Morphinae Hydrobromidum.**  $C_{17}H_{19}O_2N, HBr, 2H_2O = 402.1$ .

*Dose.*— $\frac{1}{2}$  to  $\frac{1}{2}$  grain (0.008 to 0.03 g.).

A white powder, soluble 1 in 22 of water and about 1 in 50 of alcohol 90%. Given with hydrobromic acid as sedative.

**[D-P1-81] Morphinae Hydrochloridum (B.P., Fr. Cx., P.G. VI, P. Helv. V, P. Dan., P. Ital. V, F.E. VIII, P. Belg. IV).**

$C_{17}H_{19}O_2N, HCl, 3H_2O = 375.7$ .

*Dose.*— $\frac{1}{2}$  to  $\frac{1}{2}$  grain (0.008 to 0.02 g.), which may be increased.

In silky white crystals or in powder. **Soluble** 1 in 25 of water, about 1 in 50 of alcohol 90%, and about 1 in 8 of glycerin; insoluble in ether or chloroform.

**[D-P1-81] Hypodermic Tablets** contain  $\frac{1}{2}$ ,  $\frac{1}{4}$ ,  $\frac{1}{8}$ ,  $\frac{1}{16}$  and 1 grain.

**[D-P1-81] Guttæ Morphinae et Cocainæ (Aural).** Morphine hydrochloride 4 gr., cocaine hydrochloride 24 gr., glycerin 1 drachm, distilled water to  $\frac{1}{2}$  oz.

**[D-P1-81] Injectio Morphinae (B.P.C.).**

*Dose.*—5 to 10 minims (0.3 to 0.6 g.).

Contains 2½% of morphine hydrochloride (about  $\frac{1}{2}$  gr. in 10 m.).

**[D-P1-81] Soluté Injectable de Chlorhydrate de Morphine (Fr. Cx.)** is 1%. Solutio Morphini Hydrochloridi (P. Svec. X) is 3%.

**[P1] Linctus Morphinae (U.C.H.).**

Solution of morphine hydrochloride 3 m., emulsion of chloroform 3 m., treacle 60 gr., water to 1 dr. May be more agreeably flavoured with syrup of lemon.

*Dose.*—A teaspoonful 3 or 4 times a day; repeated frequently when cough is troublesome. Taken undiluted, swallowed very slowly. *For children* of 8 to 14 years, dose 10 to 20 drops. Not suitable for very young children or in difficulty of expectoration in bronchitis.

**[P1] St. M. H.** has solution of morphine hydrochloride 10 m., honey  $\frac{1}{2}$  dr., water to 1 dr.

**[P1] Linct. Morph. (N.I.F.).** Solution of morphine hydrochloride 5 m., syrup of tolu 30 m., water to 1 dr.

**[P1] Linct. Morph. (P.M.H.).** Solution of morphine hydrochloride 15 m., syrup of tolu 30 m., water to 1 dr.

**[P1] Linct. Morph. Rub. (N.I.F.).** Solution of morphine hydrochloride 5 m., vinegar of ipecacuanha 10 m., syrup of squill 30 m., solution of bordeaux B  $\frac{1}{2}$  m., glycerin to 1 dr.

**[D-P1-81] Liquor Morphinae Hydrochloridi (B.P.).**

*Dose.*—5 to 30 minims (0.3 to 2 ml.). 30 m. contains about  $\frac{1}{2}$  gr. of morphine hydrochloride.

Morphine hydrochloride 1, dilute hydrochloric acid 2, alcohol 90% 25, distilled water to 100.



**[P1] Mistura Morphinae et Phenazoni Composita.**

*Dose.*—1 ounce (30 ml.).

Solution of morphine hydrochloride 10 m., phenazone 10 gr., tincture of castor 20 m., spirit of chloroform 10 m., mucilage *q.s.*, water to 1 oz.

This is virtually a specific for spasmodic dysmenorrhœa.

**[P1] Mist. Tuss. Hydrocyan. (N.I.F.). Syn. BROMPTON MIXTURE.**

Solution of morphine hydrochloride  $7\frac{1}{2}$  m., dilute hydrocyanic acid 2 m., syrup of tolu 30 m., acid infusion of roses to  $\frac{1}{2}$  oz.

**[P1] Mist. Tuss. Rub. (N.I.F.). Syn. MIST. TUSS. ACID.**

Solution of morphine hydrochloride 5 m., vinegar of ipecacuanha 10 m., syrup of squill 30 m., solution of bordeaux B  $2\frac{1}{2}$  m., chloroform water to  $\frac{1}{2}$  oz.

**[D-P1-S1] Suppositorium Morphinae (B.P.).** Unless otherwise stated contains  $\frac{1}{2}$  grain (0.015 g.) of morphine hydrochloride in oil of theobroma *q.s.* to 15 grains.

**[P1] Syrupus Morphina (Fr. Cx.)** contains morphine hydrochloride 0.05%, water 0.95%, cold-prepared syrup to 100%.

**[P1] Trochisci Chlorodyn (B.P.C.)** contain  $\frac{1}{8}$  gr. of morphine hydrochloride (equivalent to about 8 m. of tincture of chloroform and morphine).

**[P1] Trochisci Morphinae (B.P.C.)** contain  $\frac{1}{32}$  gr. of morphine hydrochloride.

**[P1] Trochiscus Morphinae et Ipecacuanhae (B.P.).**

Contains  $\frac{1}{32}$  grain (0.002 g.) of morphine hydrochloride, with  $\frac{1}{16}$  grain (0.006 g.) of powdered ipecacuanha. Useful to allay cough.

**[D-P1-S1] Morphinae Meconas. Syn. MORPHINE BIMECONATE.**

$(C_{17}H_{19}O_5N)_2 \cdot C_7H_5O_2 \cdot 5H_2O = 860.4$ .

*Dose.*— $\frac{1}{2}$  to  $\frac{1}{4}$  grain (0.008 to 0.03 g.).

This, one of the natural salts of morphine in opium, is in white minute acicular crystals, soluble 1 in 34 of water.

**[D-P1-S1] Liquor Morphinae Bimeconatis.**

*Dose.*—5 to 40 minims (0.3 to 2.4 ml.).

Morphine  $14\frac{1}{2}$  gr., meconic acid 12 gr., alcohol (90%) 1 oz., mix and add distilled water to 4 oz. Filter. 1 ounce contains about 6.3 gr. or 1.45% (*w/v*) of morphine meconate. It is about the same strength as tincture of opium.

**Acidum Meconicum.**  $C_7H_5O_2 \cdot 3H_2O = 254.1$ . White crystals slightly soluble in water. A dicarboxylic hydroxy acid forming soluble salts with opium alkaloids. It occurs in good opium to extent of 5 to 8%. Has little physiological action.

**[D-P1-S1] Morphinae Sulphas (B.P.C., U.S.P. XI).**

$(C_{17}H_{19}O_5N)_2 \cdot H_2SO_4 \cdot 5H_2O = 758.5$ .

*Dose.*— $\frac{1}{2}$  to  $\frac{1}{4}$  grain (0.008 to 0.02 g.).

In white, silky acicular crystals. Soluble 1 in 21 of water, very slightly in alcohol 90% (about 1 in 700).

**[D-P1-S1] Hypodermic Tablets** contain  $\frac{1}{8}$ ,  $\frac{1}{16}$ ,  $\frac{1}{32}$ ,  $\frac{1}{64}$  and 1 grain; also combined with hyoscine hydrobromide for scopolamine-morphine narcosis, and with atropine as follows:—

{ Morphine sulphate  $\frac{1}{8}$ ,  $\frac{1}{16}$ ,  $\frac{1}{32}$ ,  $\frac{1}{64}$ ,  $\frac{1}{128}$  gr. }  
{ Atropine sulphate  $\frac{1}{160}$ ,  $\frac{1}{320}$ ,  $\frac{1}{640}$ ,  $\frac{1}{1280}$ ,  $\frac{1}{2560}$  gr. }

Morphine and atropine are given before anæsthesia, effected by gas and ether, to lessen the amount required and to minimise the secretion from the mouth and lungs.

**[D-P1-S1] Morphine Tartras (B.P.).** $(C_{17}H_{19}O_2N)_2 \cdot C_4H_6O_6 \cdot 3H_2O = 774.4$ .*Dose*.— $\frac{1}{2}$  to  $\frac{1}{4}$  grain (0.008 to 0.02 g.).

In small white nodular tufts of acicular crystals, readily **soluble** 1 in 11 of water, slightly in alcohol 90%; insoluble in ether or chloroform.

**[D-P1-S1] Liquor Morphine Tartratis (B.P.C.).***Dose*.—5 to 30 minims (0.3 to 2 ml.). 1%.

**[P1-S1] Æthylmorphine Hydrochloridum (B.P.C., P. Hung., P. Svec., P. Jap. V, Fr. Cx., U.S.P. XI, P.G. VI, P. Ned. V, P. Belg. IV, P. Helv. V, P. Dan., P. Ital. V). Prop. Name. DIONIN (Merck, Darmstadt; Savory & Moore, London).**  
 $C_{19}H_{23}O_3N \cdot HCl \cdot 2H_2O = 385.7$ .

**[P1]** "Alkaloids, the following; their salts, simple or complex:—*Ethylmorphine*."

**[S1]** "Alkaloids, the following; their salts, simple or complex:—*Ethylmorphine*, except substances containing less than 0.2% of *ethylmorphine*."

**NOTE.**—Although ethylmorphine and its salts are controlled by the *Methylmorphine and Ethylmorphine Regulations, 1933*, these regulations do not affect any sale or distribution of the drugs by any person other than a wholesaler or any sale or distribution by an authorised seller of poisons in the course of any retail business (see p. 1145).

*Dose*.— $\frac{1}{10}$  to  $\frac{1}{2}$  grain (0.006 to 0.03 g.), by the mouth;  $\frac{1}{24}$  to  $\frac{1}{8}$  grain (0.0025 to 0.008 g.), by hypodermic injection. *Fr. Cx.* has max. dose in 24 hours 3 grains (0.2 g.); *P.G. VI* 5 grains (0.3 g.).

A white crystalline powder, m.p. about 123°, obtained by the action of diethyl sulphate on morphine in alkaline alcoholic solution and recrystallisation from hydrochloric acid. Morphine contains one phenolic and one alcoholic group. In ethylmorphine the H of the phenolic group is replaced by  $C_2H_5$ .

**Soluble** about 1 in 10 of water, 1 in 25 of alcohol 90%; insoluble in ether and chloroform.

**Uses.** To replace codeine and morphine in bronchitis, pulmonary emphysema and bronchial asthma, and for whooping-cough.

A useful anodyne in glaucoma, iritis, corneal ulcers, etc., and is of service in interstitial keratitis with potassium iodide internally and yellow precipitate ointment in the conjunctival sac. Solutions may be from 1 to 5% strength or more, but it may cause "ophthalmic fireworks," pain, chemosis, swelling and sneezing. The 5% solution is of value in clearing up corneal opacities.

**[P1-S1] Elixir Æthylmorphine et Terpini (B.P.C.).***Dose*.— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Contains  $\frac{1}{8}$  gr. of ethylmorphine hydrochloride and  $\frac{5}{18}$  gr. of

terpin hydrate in alcohol 90%, glycerin and syrup of wild cherry to 1 drachm.

[P1-S1] **Gutt. Ethylmorphin.** (N.I.F.). Ethylmorphine hydrochloride 3 gr., distilled water to 2 fl. dr.

[P1-S1] **Guttæ Ethylmorphinæ Hydrochloridi** (R.L.O.H.). *Syn.* GUTTÆ DIONINÆ.

Contain 4, 8, 20 or 40 gr. of ethylmorphine hydrochloride in 1 oz. of sterilised water.

**Diamorphinæ Hydrochloridum** (B.P.). *Syn.* DIACETYLMORPHINE HYDROCHLORIDE (P.G. VI, P. Helv. V, P. Dan., Fr. Cx., P. Jap. V), HEROIN HYDROCHLORIDE.  
 $C_{21}H_{23}O_5N \cdot HCl \cdot H_2O = 423.7$ .

[D] "*Diacetylmorphine and its salts, any preparation, admixture, extract or other substance containing any proportion of diacetylmorphine.*"

[P1] and [S1] "*Alkaloids, the following; their salts, simple or complex:—Diacetylmorphine.*"

The manufacture and importation of heroin are prohibited in the United States and its use is actively discouraged in many other countries.

**Dose.**— $\frac{1}{12}$  to  $\frac{1}{8}$  grain (0.0025 to 0.008 g.). P.G. VI, P. Helv. V and P. Dan. have max. in 24 hours approx.  $\frac{1}{4}$  grain. Fr. Cx.,  $\frac{1}{8}$  grain.

A colourless crystalline powder, m.p.  $229^{\circ}$  to  $233^{\circ}$ , obtained by the action of acetic anhydride on morphine. The hydrogen atoms of both the alcoholic and phenolic OH groups are replaced by the  $CH_3 \cdot CO$  group.

**Soluble** about 1 in 2 of water and about 1 in 11 of alcohol 90%.

**Incompatibles.** Both alkalis and acids and other chemicals as morphine.

**Antidotes.** Treat as for poisoning by morphine, *see* p. 697. Recovery after 9 grains is on record.

**Heroin and Morphine Addiction.** Heroin is used sometimes by injection and sometimes as a snuff like cocaine. The addict prefers it to morphine. The morphine addict has only one or two stools a week, whereas the bowels of the diamorphine addict are almost normal. There is not so much pallor or emaciation.

Of 200 addicts in Egypt, 138 used heroin, 20 opium, 14 hashish, 12 morphine, 8 manzûl (a mixture of hashish, dry spices and herbs), 6 mixtures and 2 cocaine. Owing to the transmission of malaria in 1929 the intravenous route fell into disrepute, and heroin is now usually taken by snuffing, the average dose being 1 to 2 gr. daily. Description of a 7-day special substitution treatment employing morphine, phenobarbitone, intramuscular magnesium sulphate and paraldehyde.—A. G. Biggam and co-workers, *Lancet*, i/1932, 923.

Whereas in 1932 the number of heroin, cocaine, opium and hashish addicts in Egypt were 5695, 714, 7141 and 18,871 respectively, in 1934, as a result of the work of the Egyptian Central Narcotics Intelligence Bureau, the figures were reduced to 1605, 279, 5237, and 11,552 respectively, or a reduction of from 0.23% of the total population to 0.133%.—E. W. Adams, *Bull. Hyg.*, 1936, 341.

**Uses.** Often more effectual than morphine in relief of severe nerve pain but is more dangerous. It does not constipate. The danger of addiction from its continual use must never be forgotten. Sedative for cough without much expectoration, *e.g.*, in phthisis,

bronchitis, and laryngitis, also in asthma. Has been given in hæmoptysis.

Although diamorphine (hypodermically) is preferable to morphine for relief of pain after abdominal operations, care should be taken to see that the patient is *fully round from the anæsthetic before administering*, and only  $\frac{1}{2}$  gr. should be given, repeated if necessary, as the effect of larger doses may be very dangerous to the respiratory centre. Artificial respiration necessary in two cases.—A. E. M. Woolf, *Brit. med. J.*, i/1929, 499; see also *ibid.*, 975.

[D-P1-81] **Elixir Diamorphinæ et Pini Compositum** (B.P.C.).

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Contains about  $\frac{3}{8}$  gr. of diamorphine hydrochloride,  $\frac{5}{8}$  gr. of terpin hydrate and  $\frac{1}{2}$  m. of oil of pumilio pine in 1 dr.

[D-P1-81] **Elixir Diamorphinæ et Terpini** (B.P.C.).

*Dose.*— $\frac{1}{2}$  to 1 drachm.

Contains about  $\frac{1}{8}$  gr. of diamorphine hydrochloride and  $\frac{1}{8}$  gr. of terpin hydrate in a syrup of wild cherry menstruum.

[P1-81] **Elixir Diamorphinæ et Terpini cum Apomorphina** (B.P.C.).

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.) diluted.

Contains  $\frac{1}{10}$  gr. of diamorphine hydrochloride and  $\frac{3}{8}$  gr. of apomorphine hydrochloride, with  $\frac{5}{8}$  gr. of terpin hydrate in 1 dr. (*exempt* [D]). For preparations of similar composition also *exempt* [D] see p. 1141.

This elixir keeps badly; it should be freshly prepared and stored in full bottles protected from light.

[D-P1-81] **Glycerinum Diamorphinæ** (B.P.C.).

*Dose.*— $\frac{1}{2}$  to 2 drachms (2 to 8 ml.).

Contains about  $\frac{3}{8}$  gr. of diamorphine hydrochloride in 1 drachm with acid infusion of roses in a water-alcohol-glycerin menstruum.

[D-P1-81] **Linctus Diamorphinæ** (B.P.C.).

*Dose.*— $\frac{1}{2}$  to 2 drachms (2 to 8 ml.).

Contains about  $\frac{1}{8}$  gr. of diamorphine hydrochloride in 1 dr., with tincture of hyoscyamus, syrup of wild cherry, syrup of tolu and glycerin.

[D-P1-81] **Linct. Diamorph. Hydrochlor.** (N.I.F.).

*Dose.*—1 drachm (4 ml.).

Diamorphine hydrochloride  $\frac{1}{10}$  gr., glycerin 15 m., compound solution of tartrazine  $\frac{1}{2}$  m., chloroform water to 1 dr.

[P1-81] **Linctus Diamorphinæ Camphoratus** (B.P.C.). *Syn.* ELIXIR CAMPHORÆ COMPOSITUM.

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Contains  $\frac{1}{10}$  gr. of diamorphine hydrochloride in 1 dr., with small doses of squill and ipecacuanha (*exempt* [D]).

[P1-81] **Linctus Diamorphinæ cum Ipecacuanha** (B.P.C.).

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Contains  $\frac{1}{10}$  gr. of diamorphine hydrochloride in 1 dr., with a little ipecacuanha, hyoscyamus and tolu (*exempt* [D]).

[P1-81] **Linctus Diamorphinæ et Scillæ** (B.P.C.).

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Contains  $\frac{1}{10}$  gr. of diamorphine hydrochloride in 1 dr., with  $\frac{1}{10}$  gr. of sodium antimonyltartrate and a little squill and senega (*exempt* [D]). For a preparation of similar composition also *exempt* [D] see p. 1141.

[P1-81] **Linctus Diamorphinae et Thymi** (B.P.C.). *Syn.* LINCTUS THYMI COMPOSITUS.

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Contains  $\frac{1}{10}$  gr. of diamorphine hydrochloride in 1 dr. and  $\frac{1}{2}$  gr. of apomorphine hydrochloride, with liquid extract of thyme, tolu and glycerin (*exempt* [D]).

[D-P1-81] **Pastilli Diamorphinae Hydrochloridi** contain  $\frac{1}{10}$  gr. (0.0016 g.).

[D-P1-81] **Pastilli Diamorphinae et Pini Compositi** (B.P.C.) contain  $\frac{1}{10}$  gr. of diamorphine hydrochloride,  $\frac{1}{2}$  m. of oil of pumilio pine and  $\frac{1}{4}$  gr. of terpihydrate.

[D-P1-81] **Morphine Methylbromide.** *Syn.* MORPHOSAN.

$C_{17}H_{19}O_3NBr \cdot H_2O = 398.1$ .

*Dose.*—*Hypodermically*,  $\frac{1}{4}$  to  $\frac{1}{2}$  grain (0.008 to 0.016 g.).

White needles soluble 1 in 20. Compared with morphine it is non-poisonous—it is thought to be 10 times less potent.

*Uses.* In epilepsy, also for use with hyoscine as anæsthetic.

[D-P1-81] **Morphine Methylchloride**,  $C_{17}H_{19}O_3NCl \cdot 2H_2O = 389.7$ , is a similar compound, soluble 1 in 10 of water.

The hydrochloride of this base is readily soluble 1 in 200; the sulphate 1 in 170.

[D-P1-81] **Benzylmorphinae Hydrochloridum.**

$C_{17}H_{19}O_3N(OCH_2C_6H_5) \cdot HCl = 411.7$

[D] "Benzylmorphine and its salts; any preparation, admixture, extract or other substance containing any proportion of benzylmorphine or its salts."

[P1] and [81] "Alkaloids, the following; their salts, simple or complex:—Benzylmorphine."

*Dose.*— $\frac{1}{4}$  to  $\frac{1}{2}$  grain (0.008 to 0.03 g.).

Colourless microcrystalline powder with bitter taste. Soluble 1 in 200 of water, 1 in 160 of alcohol 90%; insoluble in chloroform and ether. Similar in therapeutic properties to codeine and ethylmorphine and administered with expectorants for local irritation of respiratory organs.

**Narcotina** (B.P.C.).  $C_{18}H_{21}O_3N(OCH_3) = 413.2$ .

*Dose.*—1 to 3 grains (0.06 to 0.2 g.) or more in a pill.

An alkaloid from opium (sometimes as much as 15% is present), in white crystals, insoluble in water, soluble 1 in 3 of chloroform, 1 in 100 of 90% alcohol, 1 in 125 of ether, soluble also in benzene. An anti-periodic analogous to quinine. Has been used in malaria, but there is no clinical evidence of its therapeutic value.

**Narcotine Hydrochloride** (P. Ned. V, P. Helv. V, P. Dan.).

*Dose.*—1 to 3 grains (0.06 to 0.2 g.). White crystals soluble about 1 in 4 of water.

**Narceina.**  $C_{23}H_{27}NO_3 \cdot 3H_2O = 499.3$ .

*Dose.*— $\frac{1}{2}$  to 1 grain. An opium alkaloid soluble in alcohol, almost insoluble in water. Hypnotic sedative of doubtful utility. **Narceine Hydrochloride** (P. Ned. V, P. Helv. V). Action is similar to morphine, but it is rarely used in medicine.

[P1-81] **Papaverina** (B.P.C., F.E. VIII).  $C_{20}H_{21}O_4N = 339.2$ .

[P1] "Alkaloids, the following; their salts, simple or complex:—Papaverine."

[81] "Alkaloids, the following; their salts, simple or complex:—Papaverine, except substances containing less than 1% of papaverine."

*Dose.*—2 to 4 grains (0.12 to 0.25 g.). An alkaloid of opium (0.5 to 1%). M.p. 147°. Easily soluble in hot alcohol, but with difficulty in cold.

[P1-81] **Papaverinæ Hydrochloridum** (*P. Helv. V, Fr. Cx., P.G. VI, P. Ned. V, P. Svec. X, P. Belg. IV, F.E. VIII, P. Ital. V*).  $C_{20}H_{21}O_4N.HCl = 375.6$ .

**Dose.**—2 to 4 grains (0.12 to 0.25 g.). *P. Helv. V* has max. single dose approx. 3 grains; max. in 24 hours 10 grains; by hypodermic injection  $\frac{1}{2}$  and  $2\frac{1}{2}$  grains respectively.

A white crystalline powder slowly soluble 1 in 40 of water, giving an acid solution; also soluble 1 in 9 of chloroform and slightly soluble in alcohol. Is used for the same purposes as the sulphate.

**ARTERIAL OCCLUSION.** Slow intravenous injection of  $\frac{1}{4}$  to  $\frac{1}{2}$  gr. of papaverine hydrochloride in 1 ml. of normal saline, administered within 6 hours of the occlusion, may tide a limb over the critical period or enable operation to be performed at a time when, without the injection, the limb would be gangrenous.—G. de Takats, *per Brit. med. J. Epit.*, ii/1936, 10.

**RAYNAUD'S DISEASE.** Five patients successfully treated by means of histamine iontophoresis followed by papaverine intravenously. Histamine iontophoresis releases the spasm of the minute vessels of the skin but increases the spasm of the larger arteries. This may be counteracted by giving papaverine hydrochloride three times weekly in doses of 60 to 120 mg., usually before and after histamine iontophoresis. The treatments are continued for 8 to 12 weeks.—M. G. Mulinos *et al.*, *Amer. J. med. Sci.*, 1939, 197, 793.

[P1-81] **Papaverinæ Sulphas.**  $(C_{20}H_{21}O_4N)_2.H_2SO_4 = 776.4$ .

**Dose.**—2 to 4 grains (0.12 to 0.25 g.) *per os* or hypodermically; up to 8 grains (0.5 g.) in a day.

A white crystalline powder soluble 1 in 2 of water. It is said to be non-toxic in single doses of even 1 g.

A rather feeble central analgesic and a local anæsthetic. Does not induce a habit like morphine. In all kinds of gastric and intestinal spasms (also for the diagnosis of pyloric spasm), in biliary colic and in bronchial spasm and other forms of excitability of the involuntary muscles. Of more doubtful value in pertussis, hyperemesis and vascular spasm—angina pectoris, acute uræmia and eclampsia. Ureteral calculi have been treated by instillation through a catheter of 5 ml. of 2% solution.

**CALCULUS.** A most valuable drug for introducing into the ureter in cases of calculus. It has a local analgesic effect and its property of lowering the tonus of smooth muscle, combined with its low toxicity, warrants its more extended use.—S. F. Wildman, *per Med. Annu.*, 1938, 544.

[D-P1-81] **Spasmalgin** (*Roche Products, Welwyn Garden City*). Combination of papaverine 0.02 g., Omnopon 0.01 g. and Atrinal (a sulphonic derivative of atropine) 0.001 g. in tablet form, or in solution in ampoules. For pathological conditions due to spasm of plain muscle, *e.g.*, gastric pain, cardiac asthma, dysmenorrhœa, hiccough, renal colic and sea-sickness. **Dose.**—1 to 2 ampoules or tablets a day, increased to 4 in severe cases.

**Perparine.** A synthetic derivative of papaverine in which the four methoxy groups are replaced by four ethoxy groups. The action is stated to be similar to that of papaverine, but to be two or three times more intense with only one third the toxicity. Suggested as a morphine substitute in the treatment of conditions in which pain is produced by spasm of plain muscle. Biliary colic, cholecystitis, vesical spasm, renal calculus, asthma and dysmenorrhœa successfully treated. **Surparine**, a combination of Perparine and Novatropine (brom-methyl-homatropine), particularly efficacious.—M. G. Pouchet, *per Brit. med. J.*, i/1934, 812.

**Perparine Hydrochloride**,  $C_{21}H_{29}ON.HCl$ , is a microcrystalline powder, of faintly yellow colour, tasteless, and slightly soluble in hot water, alcohol, and

very soluble in chloroform and ether. It caused diminution in motility and tonicity of the small intestine in rabbits, and the spasm caused by pilocarpine and barium hydrochloride was quickly calmed by a dose half that required by papaverine, and the relaxing effect lasted much longer. It is much less toxic than papaverine and better tolerated. It may be given clinically in a dose of 0.12 to 0.4 g. either by mouth or injection in spasmodic conditions.—H. Goldstein, *per Practitioner*, i/1937, 546.

**Eupaverin** (*Merck, Darmstadt; Savory & Moore, London*). A synthetic compound,  $C_{15}H_{18}O_4N$ , with action similar to papaverine, but stated to be less toxic.

[P1-S1-84] **Eupaco** (*Merck, Darmstadt; Savory & Moore, London*). Combination of Eupaverin, atropine methylbromide, amidopyrine and phenobarbitone, in tablets or suppositories. For spastic conditions of smooth muscle and for obstetric cases when long and difficult labour is expected.

**Octon** (*Knoll, London*). Methyloctenylamine, an unsaturated aliphatic base, supplied in the forms of its bitartrate (in tablets containing  $2\frac{1}{2}$  gr.) and hydrochloride (in 10% solution). In its paralysing effect on the smooth musculature it is 5 to 10 times more active than papaverine and its effect is of longer duration; its toxicity is from  $1\frac{1}{2}$  to 2 times that of papaverine. *Dose*.—1 tablet or 15 to 20 drops of solution 3 times daily. Antispasmodic and anodyne in pain due to spasms. It is also supplied in ampoules of 1.1 ml. (1 ml. contains  $1\frac{1}{2}$  gr. of Octon hydrochloride) for subcutaneous or intramuscular injection.

[D-P1-81] **Thebaine Hydrochloride** (*P. Ned. V, P. Helv. V*).  $C_{15}H_{21}O_3N.HCl, \frac{1}{2}H_2O = 356.6$ .

[D] "*Thebaine and its salts; any preparation, admixture, extract or other substance containing any proportion of thebaine or its salts.*"

[P1] "*Alkaloids, the following; their salts, simple or complex:—Thebaine.*"

[S1] "*Alkaloids, the following; their salts, simple or complex:—Thebaine, except substances containing less than 1% of thebaine.*"

*Dose*.— $\frac{1}{2}$  to 1 grain *per os* increased with care; hypodermically  $\frac{1}{10}$  grain.

The salt of an alkaloid of opium, soluble about 1 in 15 of water. Has been used in neuralgic affections.

## NITROGLYCERINUM



*Syn.* TRINITROGLYCERIN, GLONIN, TRINITRIN (*Fr. Cx.*), GLYCERYLIS TRINITRAS.

[P1] "*Glyceryl trinitrate.*"

*Dose*.— $\frac{1}{200}$  to  $\frac{1}{80}$  grain (0.0003 to 0.0013 g.) increased to  $\frac{1}{10}$  grain.

Tolerance may develop to a marked degree but is of exceeding short duration. A case recorded failing to respond after 6 months' use to 500 times the initial dose.—H. B. Myers and V. T. Austin, *J. Pharmacol.*, June, 1929, 227.

Nitroglycerin is a dense, opaque, white, oily liquid, transparent when dehydrated, and of sp. gr. 1.600. It has no odour, is slightly volatile, and has a sweet, aromatic and pungent taste.

Slightly *soluble* in water, freely soluble in ether, 1 in 6 of almond oil, freely soluble in absolute alcohol, and 1 in 15 of 90% alcohol. Nitroglycerin in fatty or oily solution is perfectly safe and stable, but in alcoholic solution the substance must be handled with the utmost caution, *vide infra*.

**Incompatibility.** Nitroglycerin is decomposed by caustic alkalis. The alcoholic solution is also precipitated by water in excess.

**Antidotes.** Keep patient lying down and warm; apply ice to the head. Give 30 m. of liquid extract of ergot by mouth, repeating the dose if necessary. Ephedrine hydrochloride,  $\frac{1}{4}$  gr. hypodermically, has been recommended. Artificial respiration may be necessary.

Strychnine, ergot and belladonna are recommended to counteract the headache produced by large doses.

**Uses.** Physiologically it has the action of the nitrites and is especially valuable in angina pectoris and in asthmatic paroxysms, also generally to relieve dyspnoea of cardiac, pulmonary or renal origin. Repeated doses can be given with perfect safety but habituation quickly develops, necessitating increased dosage. Suspension of administration for a few days may restore susceptibility. It acts more quickly if taken on an empty stomach, and good results are claimed by sub-lingual administration,  $\frac{1}{10}$  gr. three to four times daily.

Nitroglycerin, within 2 minutes of taking, accelerates the pulse, dilates the arteries, produces a feeling of fullness all over the body, but particularly in the head by a throbbing at the sides of the temples. It also causes headache, which lasts from 15 minutes to several hours, according to the quantity taken; but to patients accustomed to its use the headache is not felt. In treating angina pectoris, neuralgia, asthma, migraine, sea-sickness and Bright's disease, its action is like that of amyl nitrite and the other nitrites, but its effects last much longer. For the weak heart of fatty degeneration and of old persons, this lessened tension proves valuable. It has been given in hæmoptysis but is of doubtful value. In tinnitus aurium it has been found useful. In arteriosclerosis patients are made more comfortable by small doses for a week or two.

**ANGINA PECTORIS.** From a study of 87 patients it was observed that 97% of attacks are of less than three minutes in duration. Since the attacks are of short duration the cessation of pain frequently coincides with the solution of the nitroglycerin tablet, and this may explain in part the frequency of apparently beneficial results. The tablet triturate is slow in dissolving and the nitroglycerin content does not become available until the pain has disappeared or is subsiding. The hypodermic tablet, which is more rapidly soluble, is the preparation of choice, and for all practical purposes  $\frac{1}{10}$  gr. is as effective as  $\frac{1}{100}$  gr. Nitroglycerin (or amyl nitrite) was found of no value in many patients and increased the duration of pain in a few individuals. In about one-half the patients these drugs decreased the duration of pain by about one-third.—J. E. F. Riseman and M. G. Brown, *New Engl. J. Med.*, ii/1937, 470.

**VOMITING OF PREGNANCY.** Twelve severe consecutive cases in whom all the common methods had failed were treated with uniformly good results by means of glyceryl trinitrate  $\frac{1}{100}$  gr. under the tongue 10 minutes before meals.



All of them ceased vomiting within two days of the onset of treatment. No untoward effects except transient headache.—J. M. McGowan *et al.*, *J. Amer. med. Ass.*, i/1938, 498.

**[P1] Haustus Nitroglycerini.**

Solution of glyceryl trinitrate 1 m., sodium bicarbonate 10 gr., compound tincture of cardamom 1 dr., spirit of chloroform 20 m., water to 1½ oz. To be slowly sipped at first symptoms of an attack as restorative in angina pectoris.

**[P1] Gowers' Migraine Mixture.** Sodium bromide 5 to 10 gr., solution of glyceryl trinitrate 2 m., dilute hydrobromic acid 5 m., tincture of nux vomica 5 m., tincture of gelsemium 5 to 10 m., syrup of lemon 1 dr., water to ½ oz. To be taken three times a day after food. Tincture of belladonna 5 to 10 m. can usefully be included either in addition to, or in place of, the nux vomica. This mixture must be taken for long periods in severe cases, but not during an attack. It should be supplemented by phenobarbitone ½ gr. every night and when an attack threatens.—D. Brinton, *Practitioner*, i/1936, 528.

**[P1] Injectio Nitroglycerini Hypodermica.**

*Dose.*—1 to 4 minims (0.06 to 0.25 ml.).

Solution of glyceryl trinitrate 5, alcohol (90%) 2, distilled water to 12.

Contains about  $\frac{1}{250}$  gr. in 1 m. Acts promptly and is useful in collapse, etc., when the patient cannot swallow.

**P1] Liquor Glycerylis Trinitratis (B.P., F.E. VIII, P. Hung., P.G. VI, P. Belg. IV, P. Helv. V, P. Ned. V). Syn. SOLUTIO NITROGLYCERINI SPIRITUOSA (I.A.), LIQUOR TRINITRINI (Fr. Cx.), LIQUOR NITROGLYCERINI, SPIRITUS GLYCERYLIS NITRATIS.**

*Dose.*—½ to 2 minims (0.03 to 0.12 ml.). The dose may be increased gradually to 10 minims, if necessary, every 3 or 4 hours, in any aqueous vehicle. 2 minims contains about  $\frac{1}{80}$  gr. of glyceryl trinitrate.

A 1% w/v solution of glyceryl trinitrate in alcohol 90%. *P. Ned. V* gives directions for making direct from glycerin by nitration with a mixture of nitric and sulphuric acids.

A colourless neutral liquid; 10 ml. with an equal volume of water keeps clear, but diluted further, the glyceryl trinitrate separates in oily drops, which explode when struck with a hammer. Should be kept from sunlight. A 5% and a 10% solution in absolute alcohol are also prepared commercially but are not safe for use in dispensing. A little caustic potash solution should be poured over it to decompose should it be accidentally spilled.

**[P1] Spiritus Glycerylis Trinitratis (U.S.P. XI).**

*Average dose.*—1 minim (0.06 ml.).

An alcoholic solution containing about 1% w/v of glyceryl trinitrate, and of the same strength therefore as the Liquor of the *B.P.*

**[P1] Tabella Glycerylis Trinitratis (B.P.). Syn. TABELLÆ TRINITRINI, TABLETS OF NITROGLYCERIN.**

Tablets of chocolate, each weighing 0.3 g. (5 grains), and containing 0.0005 g. ( $\frac{1}{2000}$  grain).

*Dose.*—1 or 2 tablets.

Tablets are also available containing  $\frac{1}{400}$ ,  $\frac{1}{300}$ ,  $\frac{1}{200}$ ,  $\frac{1}{100}$  and  $\frac{1}{50}$  grain. Also made with lactose instead of chocolate.

**[P1] Tabellæ Glycerylis Trinitratis (U.S.P. XI).**

*Average dose.*— $\frac{1}{2000}$  grain (0.0005 g.) of glyceryl trinitrate.

No definite weight or strength is prescribed for these tablets, but they are required to contain from 80 to 112.5% of the amount of glyceryl trinitrate stated on the label.

**[P1] Tabellæ Nitroglycerini Compositæ.**

Nitroglycerin  $\frac{1}{10}$  gr., amyl nitrite  $\frac{1}{2}$  gr., menthol  $\frac{1}{10}$  gr., capsicum  $\frac{1}{10}$  gr.

**[P1] Tabellæ Anti-Asthmaticæ (Hare).**

*Dose.*—1 to 4 thrice daily.

Nitroglycerin  $\frac{1}{10}$  gr., sodium iodide 2 gr., potassium bromide 2 gr., liquid extract of euphorbia 3 m., tincture of lobelia 4 m.

Very useful in asthma; the nitroglycerin depresses the peripheral ends of the vagus nerve and stimulates the heart by removing the inhibitory action of the vagus and relieving blood vessels elsewhere.

**[P1-S1] Tabellæ Nitroglycerini  $\frac{1}{10}$  gr. (0.0065 g.) et Strychninæ  $\frac{1}{10}$  gr. (0.0013 g.).**

In migraine, nitroglycerin, especially in combination with strychnine, is of value. It relieves headache almost immediately. Its vasodilator effect lowers blood pressure in the peripheral vessels, and so reduces cerebral and arterial pressure. In high arterial tension where the heart is beginning to fail and such symptoms as irregularity of pulse, giddiness, shortness of breath, or even œdema of ankles begin to appear, Brunton advised to combine cardiac tonics with vasodilators.

**[P1] Hypotensive Tablets (Parke, Davis, London)** contain lithium hippurate 2 gr., sodium nitrite 1 gr., nitroglycerin  $\frac{1}{10}$  gr. *Dose.*—1 to 2 tablets. For the treatment of high blood pressure.

**NUX VOMICA**

*B.P., U.S.P. XI, Fr. Cx., P. Helv. V, F.E. VIII, P. Belg. IV, P. Ital. V.*

*Syn. STRYCHNI SEMEN I.A.*

**[P1] "Nux Vomica."**

"Alkaloids, the following; their salts, simple or complex:—*Brucine; Strychnine.*"

**[S1] "Nux Vomica, except substances containing less than 0.2% of strychnine."**

"Alkaloids, the following; their salts, simple or complex:—*Brucine, except substances containing less than 0.2% of brucine; strychnine, except substances containing less than 0.2% of strychnine.*"

**[S6] "Nux Vomica—specify the proportion of strychnine contained in the preparation."**

*Dose.*—*U.S.P. XI* has average dose  $1\frac{1}{2}$  grains (0.1 g.). The *B.P.* requires that when *Nux Vomica* is prescribed, *Nux Vomica Pulverata* shall be dispensed.

The dried ripe seeds of *Strychnos Nux-Vomica* (*Loganiaceæ*), imported from India and Ceylon, containing not less than 1.2% of strychnine.

**Antidotes.** Treat as for poisoning by strychnine, see p. 929.

**Uses.** A bitter stomachic and tonic. Stimulates the bowels, hence added to aperients. Increases nervous energy. Is employed in dyspepsia and as a general tonic in all conditions of debility and neurasthenia. For the aged, this and strychnine have been described as the only suitable bitter tonics.

In phosphaturia, small doses of *nux-vomica* and dilute hydrochloric acid are said to be of service.

[P1-81] **Extractum Nucis Vomicae Siccum (B.P.).** *Syn.* EXTRACTUM NUCIS VOMICÆ.

*Dose.*— $\frac{1}{2}$  to 1 grain (0.016 to 0.06 g.).

Contains 5% of strychnine, adjusted with calcium phosphate; 1 grain contains about  $\frac{1}{10}$  grain of strychnine.

*Fr. Cx.* conforms with *I.A.* (*Second*) making the preparation 16% of total alkaloids, with *max. single dose*  $\frac{3}{8}$  grain and *max.* in 24 hours  $1\frac{1}{2}$  grains approx. Elsewhere abroad the extract is called Extractum Strychni. *P.G. VI, P. Ital. V, F.E. VIII and P. Belg. IV* also agree with *I.A.* (*Second*).

[P1-81] **Extractum Nucis Vomicae (U.S.P. XI).**

*Average dose.*— $\frac{1}{2}$  grain (0.015 g.).

Contains 7.4% of strychnine, and is therefore 50% stronger than the dry extract of the *B.P.*

[P1-81] **Extractum Nucis Vomicae Liquidum (B.P.).**

*Dose.*—1 to 3 minims (0.06 to 0.2 ml.).

Prepared by percolating the seeds in powder with alcohol 70%, defatting with hard paraffin, and adjusting the strength so that the extract contains 1.5% *w/v* of strychnine. 3 minims contains about  $\frac{1}{10}$  grain. *P. Ital. V* has 2.5% of alkaloids.

[P1] **Mist. Gent. Acid. c. Nuc. Vom. (N.I.F.).** Dilute hydrochloric acid 10 m., liquid extract of nux vomica  $1\frac{1}{2}$  m., concentrated compound infusion of gentian 15 m., chloroform water to  $\frac{1}{2}$  oz.

[P1] **Mist. Nuc. Vom. Alk. (N.I.F.).** Sodium bicarbonate 10 gr., liquid extract of nux vomica  $1\frac{1}{2}$  m., chloroform water to  $\frac{1}{2}$  oz.

[P1] **Mist. Nuc. Vom. c. Gent. (N.I.F.).** Sodium bicarbonate 10 gr., liquid extract of nux vomica  $1\frac{1}{2}$  m., concentrated compound infusion of gentian 15 m., chloroform water to  $\frac{1}{2}$  oz.

[P1-81] **Nux Vomica Pulverata (B.P.).** *Syn.* PULVIS NUCIS VOMICÆ.

*Dose.*—1 to 4 grains (0.06 to 0.25 g.). 4 grains contains about  $\frac{1}{10}$  grain of strychnine.

Nux vomica in fine powder adjusted by admixture with stronger or weaker nux vomica, or with lactose, to contain 1.2% of strychnine.

[P1] **Tinctura Nucis Vomicae (B.P.).**

*Dose.*—10 to 30 minims (0.6 to 2 ml.), often less.

Liquid extract of nux vomica 8.34% *v/v*, with alcohol 90% and distilled water. It contains 0.125% *w/v* of strychnine; 30 minims contains about  $\frac{1}{10}$  grain.

*I.A.* (*Second*) recommended 0.25% of total alkaloids. *P. Belg. IV, F.E. VIII and P. Ital. V* conform to this standard.

*Fr. Cx.* prepares by dissolving 1.562 g. of extract (*Fr. Cx.*) in alcohol 70% *q.s.* to produce 100 g. This contains 0.25% of combined alkaloids (*I.A.*). *Max. single dose*, 1 g.; *max.* during 24 hours, 5 g.

**PSYCHONEUROSIS.** Most sufferers from functional nervous illness are considerably benefited by a mixture such as the following, which is best styled a sedative tonic: sodium bromide 5 gr., tincture of nux vomica 5 to 10 m., spirit of chloroform 10 m., compound infusion of gentian to  $\frac{1}{2}$  oz. *Dose.*— $\frac{1}{2}$  oz. thrice daily, after meals.—D. Brinton, *Fractitioner*, 1/1936, 524.

**[P1] Tinctura Nucis Vomice (U.S.P. XI).**

*Average dose.*—15 minims (1 ml.).

Prepared by maceration with a mixture of hydrochloric acid, alcohol and water, followed by percolation with a diluted alcohol and adjusting the volume to contain 0.115% w/v of strychnine; the tincture is then cooled to 5° for  $\frac{1}{2}$  hour and filtered.

**[P1-81] Ignatia (B.P.C.). Syn. ST. IGNATIUS BEAN (Fr. Cx.).**

*Dose.*— $\frac{1}{4}$  to 2 grains (0.03 to 0.12 g.).

The dried ripe seeds of *Strychnos Ignatii* (Loganiaceæ), containing strychnine and brucine, the alkaloidal content being 2.5 to 3%, of which rather more than half is strychnine. A nerve tonic similar in action to nux vomica.

*Antidotes.* Treat as for poisoning by strychnine, see p. 929.

**[P1] Tinctura Ignatiæ (B.P.C.).**

*Dose.*—5 to 20 minims (0.3 to 1.2 ml.). 1 in 10.

**[P1-81] Teinture de Fève de Saint-Ignace Composée (Fr. Cx.). Syn. GOUTTES AMERES DE BAUMÉ.**

*Dose.*—Max. single 4 minims; max. during 24 hours 30 m., approximately.

Prepared by macerating 1 of ignatia and 0.025 of potassium carbonate in 5 of alcohol 70%.

**[P1-81] Cabalonga de Tabasco (P. Mex. V). Mata-perros, Veneno del diablo.**  
The seeds of *Strychnos triplinervia*. According to Professor Graham, they contain 1.83% of strychnine and brucine. Used in place of ignatia.**Damiana (B.P.C.). Syn. TURNERA, HYSTERIONICA, BAYLAHUEN.**

The dried leaves of *Turnera diffusa* var. *aphrodisiaca* (Turneraceæ) and probably other species. Contains a bitter principle, damianin, resins and  $\frac{1}{2}$  to 1% of volatile oil. Is laxative and tonic, and is reputed to have aphrodisiac properties.

**Extractum Damianæ (B.P.C.).**

*Dose.*—5 to 10 grains (0.3 to 0.6 g.). A soft extract.

**Extractum Damianæ Liquidum (B.P.C.).**

*Dose.*— $\frac{1}{4}$  to 1 drachm (2 to 4 ml.). 1 in 1.

**[P1] Mistura Damianæ Compositum (B.P.C.).**

*Dose.*—1 to 2 drachms (4 to 8 ml.).

Contains  $\frac{1}{2}$  dr. of liquid extract of damiana, 2 m. of liquid extract of nux vomica and calcium and sodium hypophosphites in chloroform water to 2 dr.

**[P1-81] Pilulæ Damianæ Compositæ (B.P.C.).**

*Dose.*—1 pill.

Contain extract of damiana 2 gr., phosphorated suet  $\frac{1}{10}$  gr., and dry extract of nux vomica  $\frac{1}{10}$  gr.

## ŒSTRADIOL

(with other ŒSTROGENS, PROGESTERONE and the ANDROGENS)

Sex hormones are closely related to each other in their chemical structure, which resembles that of the steroids of the suprarenal cortex and other tissues of the body. They possess, likewise, physiological properties common to each other which forbid any sharp differentiation. They may, however, be broadly classified as œstrogens (the œstrus-provoking hormones), progesterone (the hormone of the corpus luteum), and androgens (the male sex hormones).

Before the isolation of the œstrogens and progesterone, desiccated preparations of the ovaries were used in the treatment of various

diseases of menstruation, disturbances of the climacteric and in hæmophilia. The preparations which were used included "Ovarian Substance," consisting of the whole ovary, "Corpora Lutea," prepared from the yellow bodies formed in the ovaries after ovulation, and "Ovarian Residue," the substance of the ovaries remaining after removal of the corpora lutea, all of which were supplied in a dried and powdered form. These preparations, being unstandardised and of doubtful value, should be replaced by the standardised preparations of the respective hormones, which are now available.

In 1923 Allen and Doisy showed that an alcoholic extract of the ovary was capable of producing œstrus in rats and mice after their ovaries had been removed. The active principle of this substance was called "œstrin," indicating that it was a substance capable of producing œstrus or heat in animals. Owing, however, to the complex nature of the fatty substances extracted from the ovaries, purification and identification of the active materials could not be achieved, and no real progress was made until Aschheim and Zondek in 1927 demonstrated the presence of œstrogenic substances in large quantities in human pregnancy urine in what was probably a purer condition than that obtained from ovaries. Pregnant mares' urine was then found to contain very large quantities and to be a convenient source of supply. In 1929 Doisy in America and Butenandt in Germany isolated from pregnancy urine a pure crystalline sex hormone which was called œstrone, and this was followed shortly after by the isolation, by Marrian, of a second hormone, œstriol. It was then found that hydrogenation of œstrone resulted in the formation of a dihydro derivative five times as active as œstrone. This substance was termed "œstradiol." Two years later, in 1935, œstradiol was separated from sow ovaries and from pregnant mares' urine, and it is this substance which is believed to be the naturally-occurring œstrus principle, œstrone and œstriol being degradation products. Estradiol is developed in both the Graafian follicles and in the non-follicular cells of the ovary, possibly by the corpus luteum. The substances œstradiol and œstrone, together with other substances of known œstrogenic activity such as equiline and equilenine, also obtained from pregnant mares' urine, probably represent the active principles of the material formerly known as "œstrin," a term which, since it does not imply any definite chemical substance, has now fallen into disuse. Criticism has also been directed against the term "œstrogenic" in that it implies a limitation of the biological activity of these substances, which in addition to provoking œstrus, also possess actions which are not related to the œstrus cycle, such as the feminisation of the plumage of birds. The alternative word "gynæcogen" has been suggested as a more suitable generic term for the members of this group.

**Esters.** Various esters of œstradiol and its derivatives have been biologically tested in an endeavour to find a product which

would be absorbed more slowly than the hormones themselves. Among those which have been prepared are the acetates, benzoates, and propionates, of which the benzoates, particularly that of œstradiol have proved to be very suitable for the purpose, giving a much more prolonged action than the free hormone and resembling more closely the continuous secretion of the natural substance as it takes place in the body. Other derivatives have also been investigated, including ethinyl œstradiol which is stated to possess great activity when given by mouth. Preparations of œstrogenic hormones for injection are usually prepared from œstradiol benzoate, whilst tablets for oral use generally consist of œstrone which is active when given by mouth.

**Standardisation.** The œstrogens are standardised on their œstrus-provoking property. When they are administered to rats or mice from which the ovaries have been removed they bring about easily recognised changes in the vaginal epithelium, and by comparison with the effect produced by the international standard preparations the strength of the test preparation can be expressed in international units. Two international standards have been set up. They consist of crystalline samples of œstrone and œstradiol benzoate. The *international unit of œstrone* is defined as the specific œstrus-producing activity of 0.0001 mg. of the standard preparation of œstrone, whilst the *international benzoate unit* is defined as the specific œstrus-producing activity of 0.0001 mg. of the standard preparation of œstradiol monobenzoate. It may be noted that the benzoate unit represents a considerably greater activity than the œstrone unit.

**Synthetic Œstrogenic Substances.** Although extensive attempts have been made to synthesise œstradiol and its derivatives, little success has been met with owing to the complexities of their chemical structure and to the stereo-isomerism which a number of them exhibit. Œstradiol, for example, exists in two stereo-isomeric forms,  $\alpha$  and  $\beta$ , only the former of which has œstrogenic activity to any degree. It was shown, however, that œstrogenic activity was not dependent upon the presence of the phenanthrene ring structure possessed by the hormones, and the search for synthetic compounds turned to relatively simple substances. It culminated in the synthesis of a derivative of stilbene, 4:4'-dihydroxy- $\alpha$  :  $\beta$ -diethylstilbene, which was found to be very highly active. This substance, generally known as diethylstilbœstrol or stilbœstrol, is three or four times as potent as œstrone when injected subcutaneously and nearly as active orally as when given by the subcutaneous route, thus differing from the natural products which are relatively inactive when given by mouth. Stilbœstrol has been tested both experimentally and clinically, and appears to be capable of replacing all the known functions of the naturally occurring œstrogenic substances. Further work on synthetic œstrogenic substances has led to the discovery of the dihydro derivative of stilbœstrol called hexœstrol,

which has been obtained as a crystalline substance capable of producing oestrus in animals. Its effects resemble those of stilboestrol, but while clinical trials indicate that it is slightly less active, it has the advantage of being more readily tolerated.

**Comparisons of Activity of Oestrogens.** Although all the follicle-stimulating preparations possess similar therapeutic properties they vary considerably in the intensity and duration of their action. Generally speaking, it may be said that the oestrogenic activity is less marked and less prolonged with oral therapy than with parenteral therapy, and that oral use necessitates the administration of amounts from five to thirty times as great as would be required to produce the same effect by injection. Thus, when given by the oral route, *oestrone* is rapidly absorbed and excreted and therefore has a low specific action. Nevertheless, owing to the convenience of oral therapy it is widely employed in this manner, and is undoubtedly effective provided it is given in adequate amounts in two or three divided doses daily. *Oestriol*, which is more effectively absorbed by the oral route, is claimed to give better results than *oestrone*.

For more intensive treatment than can conveniently be achieved by oral administration *oestrone* may be given by injection, since it is stated to be five times as active by this route. Even by injection, however, it is no more active than *oestradiol* by mouth and is much less active and has a less prolonged action than *oestradiol benzoate* by injection. In view of the fact that the esterification of an oestrogen prolongs the duration of its activity, it might be anticipated that *oestrone benzoate* would have a similarly prolonged action to *oestradiol benzoate*, but its effect is delayed until it has undergone hydrolysis in the body and *oestrone* is more effective than its benzoate. By virtue of its greater oil-solubility and slower absorption-rate, however, *oestradiol benzoate* is more suited to intensive parenteral therapy than *oestrone*, its effectiveness lasting at least three days, so that twice weekly injections may be expected to produce a continuous effect. *Oestradiol propionate* by parenteral injection is said to have an even more prolonged effect than *oestradiol benzoate*.

It has been shown that the administration of an oestrogen (crystalline *oestrone*) in the form of a tablet implanted subcutaneously leads to a prolongation of the period of effectiveness of some months; this method of administration is, however, at present only in the experimental stage.

As a general guide, it may be said that the bulk of clinical evidence favours the use of *oestrone* (or, more recently, one of the synthetic equivalents, *q.v.*) by the mouth for low intensive therapy and of *oestradiol benzoate* by injection for high intensive therapy.

**Uses.** The follicular hormone can be employed to increase the growth of the secondary sex characters and to condition the genital tract, and particularly to produce the changes in the

endometrium characteristic of the post-menstrual phase (*i.e.*, those changes which facilitate the fertilisation of the ovum) and to influence the growth of the uterus and increase its contractility. Its main indications, therefore, may be summarised as:—(1) arrest or retardation of puberty, *e.g.*, primary amenorrhœa; (2) disturbances of menstruation, *e.g.*, secondary amenorrhœa, menorrhagia and spasmodic dysmenorrhœa; (3) disturbances of the menopause and post-menopausal disorders.

The most satisfactory response is seen in the menopausal syndrome, for which it is claimed to be the ideal method of treatment. Relatively small doses of œstrone given daily by mouth control the flushing, palpitation, headaches and giddiness, and induce a general feeling of well-being. Some of the later results of the climacteric ovarian deficiency, *e.g.*, disorders of the vagina and vulva, such as pruritus, kraurosis, atrophic vulvitis, and senile vaginitis and ulceration, require higher doses of the hormone by injection. Thus, in the first two weeks of treatment doses of 100,000 i.b.u. of œstradiol benzoate are given weekly, subsequently reduced to 20,000 units weekly. Good results are also obtained, both by oral and parenteral administration, in the psychological disorders associated with the menopause, *e.g.*, in involutional melancholia, in the migraine which frequently occurs at this period, and in what is known as climacteric arthritis.

Primary amenorrhœa (delayed puberty), as also the milder forms of menstrual irregularity such as hypomenorrhœa or oligomenorrhœa, may often be completely cured by the oral administration of œstrone, and a certain percentage of cases of secondary amenorrhœa may be permanently benefited by injection therapy, but primary amenorrhœa in patients over 20 and secondary amenorrhœa of long-standing rarely, if ever, respond permanently to this therapy, the amenorrhœa returning when the treatment is suspended.

By virtue of the fact that it is responsible for the growth of the uterus and for maintaining the tone of the uterine muscle, the œstrogenic hormone may be employed with a considerable measure of success in the treatment of uterine hypoplasia, uterine inertia, and missed abortion. For these purposes it is necessary to give adequate injections of œstradiol benzoate.

œstrone is also concerned in the growth of the mammary gland and may be successfully employed for the development of under-sized breasts, being especially effective when administered by inunction, an amount of ointment containing a total of 2500 i.u. of œstrone, or 10,000 i.b.u. of œstradiol benzoate, being rubbed well into the breasts twice daily. In the treatment of persistently painful and lumpy breasts, a relatively high dosage by injection of œstrone or œstradiol benzoate has been found of value, and may often bring about sufficient improvement to avoid the necessity for operation.

œstrogenic substances, by inhibiting the secretion of the lactogenic hormone of the pituitary, suppress lactation, and large



amounts of œstradiol benzoate injected daily during the puerperium inhibit lactation and breast engorgement.

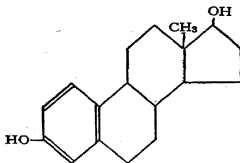
In the treatment of gonococcal vulvovaginitis in children, œstrogenic therapy now holds an established place, and is considered by many to be the most effective treatment discovered to date. Treatment would appear to be equally effective whether given by the mouth (œstrone), by injection (œstrone or œstradiol benzoate), or *per vaginam* (œstrone, in the form of suppositories), though the latter is the most favoured method. The use of œstrone suppositories has also been found of value in the treatment of leucorrhœa.

Owing to the similarity in chemical structure between the œstrogens and the carcinogenic hydrocarbons, and to the demonstration that the prolonged administration of œstrogens in high doses is capable of causing mammary cancer in susceptible strains of mice, the possibility that the therapeutic application of œstrogens might give rise to cancer in human beings was for a time seriously entertained. Subsequent work, however, has largely disposed of this fear, since it was shown that the enormous doses and the prolonged periods of administration necessary to produce cancer in mice were greatly in excess of those required to produce therapeutic effects in human beings. The use of œstrogens should, however, be avoided when a carcinoma of the breast or cervix is already present. In this connection it is of interest to note that recent work suggests that both progesterone and testosterone propionate (*q.v.*) exert an antitumorigenic action.

**œstradiol.** *Syn.* DIHYDROTHEELIN, DIHYDROXYCESTRIN, DIHYDROFOLLICULINUM (*Fr. Cx.*).  $C_{18}H_{24}O_2 = 272.37$ .

*Dose.*—0.1 to 0.2 mg. (5000 to 10,000 i.u.) daily *per os* in divided doses.

œstradiol,  $\Delta^{1,3,5}$ -œstratriene-3,17-*trans*-diol is obtained from ovaries and from the urine of pregnancy. It is a white, crystalline substance with a melting point of  $174^\circ$  to  $175^\circ$ .



Sparingly **soluble** in water; soluble about 1 in 4 of alcohol.

œstradiol reduces the number, severity and duration of "hot flushes" after a radium menopause. In nearly all of 51 cases the hormone when given by the mouth in very low dosage (not more than 0.2 mg. of œstradiol daily) the number

and severity of the flushes were reduced, and most of the less severe cases were cured. After withdrawal of the tablets there was seldom any recurrence of symptoms within the next six months.—B. C. Murless, *Lancet*, i/1939, 1205.

**Implantation of Tablets.** Under a local anæsthetic an incision 2 or 3 inches in length is made through the skin of the right or left hypogastric region; the fatty tissue is drawn apart, and each tablet (which has been previously sterilised in boiling water for 3 to 5 minutes) is embedded separately in the subcutaneous tissue. The tablets should not be in contact with one another, and should not lie directly beneath the skin, as otherwise they act too much as foreign bodies and are expelled again too easily. The deeper the tablet lies the better it will be retained; the larger the tablet the less certain the chances of healing up. A tablet one-third of an inch in diameter is most suitable for implantation, although the absorption proceeds more rapidly when the surface is larger. The skin, and on occasion the fatty tissue, is closed with a few stitches of catgut.

Estradiol was implanted subcutaneously to allow a small infantile uterus to develop and to make it ready for conception, and this was done successfully. Five tablets, each of 15 mg. were implanted deeply in the subcutaneous fat of the right hypogastric region.—A. A. Loeser, *Brit. med. J.*, i/1940, 479.

**Uterine and extra-uterine tumours** can be produced in the guinea-pig by introducing a tablet of estradiol beneath the skin. These tumours are similar to the uterine and extra-uterine fibroids or fibromyomas produced previously by a long course of injections of follicular hormones. The uterine tumours begin to appear as early as 2½ to 3 weeks after the introduction of the tablet, and the degree of tumorigenesis is much greater with the tablets than with injections of free estradiol when equal quantities are compared. The treatment with tablets is comparable, as regards the danger of tumorigenesis, to a treatment with esters of estradiol administered by injection without intervals free from treatment.—A. Lipschutz and L. Vargas, *Lancet*, i/1939, 1313.

**Estradiol Benzoate.** *Syn.* DIHYDROFOLLICULINUM BENZOICUM (*Fr. Cx.*).  $C_{25}H_{28}O_3 = 376.22$ .

*Dose.*—1 to 5 mg. (10,000 to 50,000 i.b.u.) daily by intramuscular injection.

Estradiol benzoate is prepared by the esterification of the phenolic hydroxy group of estradiol with benzoic acid. It is a white, crystalline substance melting at 194°.

**Insoluble** in water; soluble in organic solvents and oils.

**AMENORRŒA.** The rubbing of alcoholic tincture of oestrogenic hormone into the skin is almost as effective clinically as injections of the hormone, but some patients who do not react to percutaneous treatment will nevertheless react to injections. Application of oestrogenic hormone to the skin, followed by the injection of progesterone, will produce uterine bleeding in primary and secondary amenorrhœa.—B. Zondek, *Lancet*, i/1938, 1107.

**KRAUROSIS VULVÆ.** The effects of the oestrogens on senile vaginitis and kraurosis vulvæ are so great that a cure is possible without any local treatment. 5 mg. of estradiol benzoate should be injected twice weekly, and the patient is usually free from symptoms in from one to three weeks, though small doses by mouth should be continued for two or three months afterwards.—T. N. A. Jeffcoate, *Brit. med. J.*, ii/1939, 673.

**TEMPORARY POSTPONEMENT OF MENSTRUATION.** Injections of estradiol benzoate may be used to effect the temporary postponement of menstruation in order to avoid coincidence of menstrual bleeding with special events in a woman's life, such as athletic championships or marriage. Deep intramuscular injections of 50,000 i.b.u. are given every 3 to 4 days throughout the cycle, or if treatment is not begun until after ovulation may be expected to have occurred, the dosage must be increased to 100,000 i.b.u. at shorter intervals. No harmful effects are produced, and menstruation occurs 2 to 8 days after the last injection.—G. L. Foss, *Brit. med. J.*, ii/1937, 10.

The normal ovarian cycle in women can be inhibited by oestrogen (estradiol benzoate). Menstruation can be postponed for from 7 to 70 days and artificial amenorrhœa produced in this way. The dose necessary to bring about this effect is at least 70,000 i.u. Still larger doses, e.g., more than 600,000 i.u., are able to cause the uterine mucosa to react with glandular cystic hyperplasia, and pro-

tracted administration of immense doses (6,000,000 i.u. over 60 days) prevents the ripening of the follicle as well as corpus luteum formation, so that the ovaries appear to be those of an old woman. Estrogen is thus able to produce functional castration. These extremely large doses do not appear to give rise to carcinomatous changes of the uterus.—B. Zondek, *J. Amer. med. Ass.*, 1/1940, 1850.

**Oestradiol Dipropionate.**  $C_{24}H_{32}O_4$  = 384.5.

Oestradiol dipropionate is the double ester of oestradiol and propionic acid.

**Benzo-Gynœstryl** (*Roussel Laboratories, London*). Ampoules containing 1000, 10,000 or 50,000 i.b.u. of oestradiol benzoate per ml.

**Di-Menformon** (*Organon Laboratories, London*). Ampoules and solution of oestradiol benzoate for injection, containing 10,000 or 50,000 i.b.u. per ml. Also available as an ointment containing 20,000 i.b.u. per g.

**Ecto-Gynœstrol** (*Roussel Laboratories, London*). A solution of oestradiol 0.5 mg., in a mixture of equal parts of oleic alcohol and 95% ethyl alcohol. For local application only. Also available as an ointment containing 2.5 mg. of oestradiol per oz.

**Gynœstrol** (*Roussel Laboratories, London*). Tablets containing 0.025 or 0.2 mg. of oestradiol (equivalent to 1250 or 10,000 i.u.).

**Estroform Ampoules** (*British Drug Houses, London*). 1 ml. ampoules of a solution of oestradiol benzoate containing 1000, 10,000, 20,000 or 50,000 i.b.u. per ml.

**Ovocyclin** (*Ciba, Horsham*). Tablets of oestradiol containing 0.02 mg. or 0.2 mg. Also issued in an ointment containing 0.1 mg. per g.

**Ovocyclin P** (*Ciba, Horsham*). Ampoules of oestradiol dipropionate containing 1 or 5 mg. per ml.

**Progynon B Oleosum** (*Schering, London*). 1 ml. ampoules containing 10,000 i.b.u. of oestradiol benzoate in sesame oil. **Progynon B Oleosum Forte** contains 50,000 i.b.u. per ml.

**Progynon Capsules and Suppositories** (*Schering, London*), contain 0.25 mg. or 0.36 mg. of oestradiol respectively. **Progynon Ointment** contains 0.1 mg. of oestradiol per g.

**Progynon D-P** (*Schering, London*). A solution of oestradiol dipropionate for intramuscular injection.

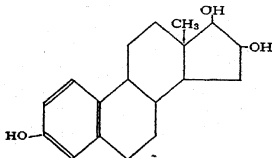
[P1] **Sedo-Gynœstryl** (*Roussel Laboratories, London*). Solution for oral administration containing per ml. 1000 i.u. of oestradiol, 0.5 g. of sodium bromide, and 0.02 g. of extract of hyoscyamus. For menopausal disturbances and ovarian hypofunction complicated with nervous symptoms. *Dose*.—50 drops daily in 4 doses for 12 to 15 days after the last period.

**Unden Ampoules (Oily)** (*Bayer Products, London*). Ampoules of an oily solution of oestradiol benzoate, containing 10,000 or 50,000 i.b.u. Also supplied in 10 ml. bottles containing 10,000 i.b.u. per ml.

**Estriol.** *Syn.* ESTRIOL, THEEOL, TRIHYDROXYOESTRIN.

$C_{18}H_{24}O_3$  = 288.37.

*Dose*.—0.05 to 0.5 mg. (500 to 5000 i.u.) daily *per os* in divided doses.



**Œstriol**,  $\Delta^{1,4,5}$ -œstratriene-3,16,17-triol, is obtained from placental tissue and pregnancy urine. It is a white, odourless, micro-crystalline powder with a melting point of  $282^\circ$ , and exhibits a reddish fluorescence under filtered ultra-violet light.

Practically *insoluble* in water; soluble in alcohol, dioxane and oils.

Face cream, stated to contain œstradiol, sold commercially and recommended for the removal of wrinkles from normal women, has decided internal effects when applied daily on the skin of experimental animals. Such treatments (a) stimulate mammary development on normal male guinea-pigs, (b) induce cornified vaginal œstrus smears in spayed female rats, (c) maintain or increase normal growth of the uterus in young or mature spayed rats, and (d) reduce the weight of testes by 80% and the weight of seminal vesicles by 90% in young male rats in comparison with normal litter mates.—C. R. Moore *et al.*, *J. Amer. med. Ass.*, ii/1938, 11.

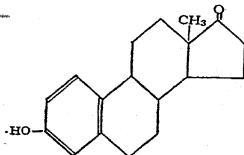
**Theelol Capsules** (Parke, Davis, London). Capsules for oral administration containing 200 or 400 i.u. of œstriol.

**Tridestrin** (Paines & Byrne, London). Tablets containing 500, 1000, or 5000 mouse units of œstriol.

**Œstrone**. *Syn.* ESTRONE, THEELIN, KETOHYDROXYCESTRIN, FOLLICULIN (*Fr. Cx.*).  $C_{18}H_{22}O_2 = 270.17$ .

*Dose.*—0.1 to 5 mg. (1000 to 50,000 i.u.) daily *per os* in divided doses or from 0.5 to 1 mg. (5000 to 10,000 i.u.) by intramuscular injection.

**Œstrone**,  $\Delta^{1,3,5}$ -œstratriene-3-ol-17-one, is obtained from the urine of pregnant mares. It is a white, odourless, crystalline powder which exhibits a strong bluish-white fluorescence under ultra-violet light.



Practically *insoluble* in water; slightly soluble in alcohol, benzene and other organic solvents; soluble about 1 in 4 of dioxane and in oils.

If œstrone is administered to men or to castrate women, from 3 to 12% of it is excreted in the urine shortly after administration. The proportion excreted is somewhat greater after oral than after parenteral administration. When given by the mouth the quantity excreted is proportional to the dose administered. Œstrone administered orally is very rapidly absorbed and excreted by the body, and has, therefore, a comparatively low specific biological action. It ought, therefore, to be given in such a form that it can be absorbed slowly and given divided into three or more daily doses.—T. Kemp and K. Pedersen-Bjergaard, *Lancet*, ii/1937, 842.

**ANXIETY STATES.** In anxiety occurring in connection with the menopause, the administration of Theelin (œstrone) intramuscularly, in doses of 1000 international rat units in oil twice weekly, gives almost uniformly good results. Where the anxiety arises apart from the menopause the effects are doubtful and may even be undesirable.—G. A. Little and D. E. Cameron, *Canad. med. Ass. J.*, ii/1937, 144.

**ATROPHIC RHINITIS.** In 31 women suffering from eczema and atrophic rhinitis, 1000 i.u. of œstrone in 0.025 ml. of olive oil was sprayed twice daily into the nose, and crusts which formed were removed by forceps twice a week. Improvement usually occurred in from 2 to 6 weeks and continued until in 20 cases there was complete disappearance of unpleasant odour, absence of crusts, disappearance of purulent secretions, and restoration of an almost normal pink mucosa.—H. Mortimer, P. R. Wright and J. B. Collip, *Canad. med. Ass. J.*, ii/1937, 445.

**BREAST ENGORGEMENT.** It is claimed that even small doses of œstrone, 2 to 6 mg. taken by mouth during the course of 3 to 6 days, are sufficient to prevent the discomfort of engorged breasts when breast feeding is contraindicated; more usually daily injections of 1 to 2 mg. of œstradiol benzoate are required.—T. N. A. Jeffcoate, *Brit. med. J.*, ii/1939, 675.

**CUSHING'S SYNDROME.** The alleged inhibitory effect of large doses of œstrone on the secretion of the anterior pituitary, suggested trial in Cushing's syndrome. Three cases received daily injections of 100,000 or 200,000 i.b.u. for periods of 40 to 50 days. No effect was obtained on the obesity, hypertrichosis, abdominal striae or hypertension, but subjective improvement occurred in all three cases, and the severe headaches were either abolished or greatly improved.—A. M. Gill, *Lancet*, ii/1937, 70.

**GONOCOCCAL VAGINITIS.** Twenty-four cases successfully treated in girls aged 2 to 9 years by nightly insertions into the vagina of capsules containing 75 rat units of Amniotin (œstrone).—R. M. Lewis and L. Weinstein, *Surg. Gynec. Obstet.*, ii/1936, 640.

All of 169 patients were cured by the use of Amniotin (œstrone) vaginal suppositories (1000 international units), one suppository being introduced daily at bedtime. There was no clinical evidence of harm due to the treatment.—R. W. Le Linde, *J. Amer. med. Ass.*, i/1938, 1633.

**INVOLUTIONAL MELANCHOLIA.** Theelin (œstrone) seems to be specific in involutional melancholia, the apparent recovery rate being 92% in a series of 14 cases. Massive doses of from 30,000 to 40,000 i.u. for the first month of treatment accelerate the recovery rate, the hospitalisation being reduced to an average period of three months.—C. C. Ault *et al.*, *J. Amer. med. Ass.*, ii/1937, 1786.

**MASTITIS.** Hormone therapy in chronic cystitic mastitis is a convenient form of palliative treatment preventing needless mutilating operations, and, if properly used, speeding regression of the disease. The results are most satisfactory in persistent painful breasts and in early adenosis. Relatively high doses of œstrogen are needed. 10,000 i.u. is injected intramuscularly twice weekly for a period of three weeks (between two menstrual periods), a total of approximately 60,000 i.u. being given. This is followed by similar doses injected once a week for another month, then twice the following month. After this, a single injection is given in the premenstruum, or capsules are taken by mouth every other day to complete six months of treatment. The oral preparation used was Amniotin in capsules containing 2000 i.u. of œstrogen each. The œstrogen is never given during menstruation and treatment is usually confined to a period of six months.—D. Lewis and C. F. Geschickter, *J. Amer. med. Ass.*, ii/1937, 1894.

**MENOPAUSAL SYMPTOMS.** In the treatment of menopausal symptoms—hot flushes, headaches, nausea and vomiting, epigastric pain, exhaustion and nervous instability—all of 76 patients were relieved and the effect in 75% of the cases was "miraculous." Theelin in oil, 2000 units, was given three times a week till symptoms were relieved, then once weekly for a varying length of time. For acute cases 4000 units may be the initial dose. It may also be necessary to increase the dosage the week before the patients would ordinarily expect their periods. The headaches and flushes disappear rapidly and the patients experience a general feeling of well-being.—M. Hilliard, *Canad. med. Ass. J.*, ii/1937, 223.

There is no doubt that in a large percentage of cases menopausal symptoms can be eliminated by the administration of estrogens. The dose required varies

considerably and can only be determined by therapeutic trial. Daily doses of 0.6 mg. of œstrone by mouth are usually sufficient, but in difficult cases intramuscular injections of 1 to 5 mg. of œstradiol benzoate every few days may also be required. Once the symptoms have been controlled, the dosage should be reduced very gradually over a period of months until the patient can manage with only 0.1 mg. once or twice weekly.—T. N. A. Jeffcoate, *Brit. med. J.*, ii/1939, 671.

**PREMATURE INFANTS.** Œstrone given orally appears definitely helpful to premature infants. The babies cause less anxiety, feeds are taken better, the initial loss of weight appears less and is usually made up sooner. The preparation used in a series of 11 premature babies was Progynon, the dose being half a dragée twice daily (i.e., 500 i.u. twice daily). One dragée was dissolved in two drachms of hot water and one drachm given as a dose. None of the babies died.—M. F. Potter, *Brit. med. J.*, i/1937, 1201.

**PRURITUS VULVÆ.** This condition can be entirely relieved by Theelin. The dose should be large and frequent (e.g., 2000 units bi-weekly), depending on the duration of the pruritus and the condition of the skin and mucous membrane of the vulva. Treatment must not be discontinued too soon, especially in older women.—M. Hilliard, *Canad. med. Ass. J.*, ii/1937, 223.

**VULVO-VAGINITIS.** In a series of 25 cases of vulvo-vaginitis of children, symptomatic and bacteriological cures were obtained in a period averaging 45 days. Recurrence of discharge occurred in 28% of cases. The method of treatment found most satisfactory was doses of 1000 international units tri-weekly.—J. V. Berry, *Canad. med. Ass. J.*, i/1937, 396.

**Implantation of Tablets.** Experimental work shows that the crystalline gonadal hormones are effective when administered by the subcutaneous implantation of solid tablets. It is concluded that the technique is particularly useful where a large-continued steady effect is required, as for instance in the depression of the gonad-stimulating and growth-promoting activity of the pituitary by estrogens, and in the masculinisation of the female by androgens. It appears that treatment of very long duration, following one administration of hormone, will be possible by implantation of tablets.—R. Deanesly and A. S. Parkes, *Lancet*, ii/1938, 606.

Female rats received tablets of œstrone implanted into the subcutaneous tissue. The tablets varied from 1 to 7 mg. in weight. Following this method of treatment, tumours were found in the mammary glands of 28 out of 49 rats. The first tumour to appear was palpable after 226 days of treatment. The tumours were frequently multiple, slowly growing, and were not near the site of the œstrone tablet.—R. L. Noble *et al.*, *Canad. med. Ass. J.*, i/1940, 413.

**Œstrone Benzoate.** *Syn.* FOLLICULINUM BENZOICUM (*Fr. Cx.*).  $C_{25}H_{36}O_2 = 374.46$ .

**Dose.**—1 to 5 mg. (10,000 to 50,000 i.b.u.) by intramuscular injection.

Œstrone benzoate is prepared by the esterification of the phenolic hydroxy group of œstrone with benzoic acid. It is a white, crystalline substance melting at about 220°.

Practically **insoluble** in water; less soluble in alcohol, but more soluble in benzene than œstrone; soluble in oils.

**Amniotin** (*Squibb, New York; Savory & Moore, London*). Preparations of œstrone available in 1 ml. ampoules each containing 2000 or 10,000 i.u. in oil, and in capsules containing 1000 or 2000 i.u. Pessaries containing 1000 i.u. are also prepared for the treatment of vulvovaginal infections in children.

**Benztone** (*Paines & Byrne, London*). 1 ml. ampoules of œstrone benzoate containing 10,000, 20,000, or 50,000 i.b.u.

**Glandubolin** (*Richter, London*). Preparations of œstrone available in ampoules containing 100, 1000, 10,000 or 50,000 i.u., and in tablets containing 100 or 1000 i.u.

**Hormotone T** (*Carnrick, Newark, N.J.; Brooks & Warburton, London*). Each tablet contains ovarian follicular hormone equivalent to 200 i.u., with thyroid  $\frac{1}{10}$  gr., and dried suprarenal and whole pituitary gland  $\frac{1}{10}$  gr. each.

**Ketodestrin** (*Paines & Byrne, London*). 1 ml. ampoules of œstrone containing 500, 1000, 5000 or 10,000 i.u.

**Kolpon** (*Organon Laboratories, London*). Soluble tablets and bougies for local application to the vagina, containing respectively 1000 i.u. and 500 i.u. of œstrone. The tablets have a buffered glucose base giving a pH of 4.0 to 4.5 on solution.

**Menformon** (*Organon Laboratories, London*). Preparations of œstrone available as an aqueous solution in 1 ml. ampoules (100 or 1000 i.u. per ml.), an oily solution in 1 ml. ampoules and 5 ml. vials (10,000 i.u. per ml.), an ointment (5000 i.u. per g.), tablets (100, 500, 1000, 3000 or 10,000 i.u. per tablet), and as drops for oral use (10,000 i.u. per ml. in oil).

**œstroform Tablets** (*British Drug Houses, London*). Tablets of œstrone containing 1000, 5000 or 10,000 i.u. per tablet. **œstroform Pessaries** contain in each 1000 i.u.

**œstroglandol** (*Roche Products, Welwyn Garden City*). Preparations of œstrone, available as tablets containing 1000 i.u., ampoules containing 1000 i.u., and ointment containing 10,000 i.u. per g.

**Ovarnon** (*Organon Laboratories, London*). Tablets containing 2.5 gr. of ovarian powder, representing 10 i.u. of œstrone.

**Ovostab Tablets** (*Boots, Nottingham*). Tablets contain 1000 or 10,000 i.u. of œstrone.

**Perlatan** (*Boehringer, Mannheim; Coates & Cooper, London*). Preparations of œstrone available for injection in 1 ml. ampoules containing 500, 1000 or 10,000 i.u., and in 10 ml. vials containing 400 i.u. per ml. Tablets containing 500 i.u., and vaginal suppositories containing 1000 i.u. are also prepared.

**Progynon Dragées** (*Schering, London*). Dragées of œstrone containing 1000, 3000 or 10,000 i.u.

**Sistomensin** (*Ciba, Horsham*). Preparations of lipo-soluble ovarian hormones, available in tablets containing  $\frac{1}{2}$  gr., and in 1 ml. ampoules containing  $\frac{1}{2}$  gr., equivalent to 10 i.u. of œstrone. *Dose*.—1 to 3 tablets three times a day, or 1 to 2 ampoules a day subcutaneously or intramuscularly.

**Solestrin** (*Paines & Byrne, London*). Alcoholic solution of œstrone for percutaneous administration. *Dose*.—10 to 20 drops (1 to 2 ml.) once or twice daily. (One drop contains 750 units of œstrone.)

**Theelin** (*Parke, Davis, London*). Ampoules of œstrone containing 200 i.u. per ml., and pessaries containing 2000 i.u. in a glycoelatin base. **Theelin in Oil**. Ampoules of œstrone containing 1000, 2000, 5000 or 10,000 i.u. per ml.

Theelin in oil stimulates development of the sex-related structures in women, producing changes in the breast, gross appearance of the vagina, with increased mucous secretion, and growth of the endometrium and vaginal mucosa in dosages as low as 5000 i.u. Relief of symptoms of castration was obtained with this dosage, but this will at the same time stimulate development of the endometrium sufficiently to cause uterine bleeding when discontinued. The large doses of theelin advocated by some (from 30,000 to 50,000 rat units) as necessary to produce the interval phase of the endometrium, are grossly excessive. Theelin in oil is much more effective than in aqueous solution. When administered intramuscularly in the human being, smaller dosages and less frequent intervals produce more rapid and more marked effect on the endometrium and vaginal mucosa.—A. A. Werner *et al.*, *J. Amer. med. Ass.*, ii/1937, 1027.

**Thelestrin** (*Carrick, Newark, N.J.; Brooks & Warburton, London*). Ampoules of œstrone containing 2000 i.u. per ml.

**Unden** (*Bayer Products, London*). Ampoules of œstrone containing 1000 i.u. per ml., or tablets for oral administration containing 1000 i.u. An ointment for local application containing 1000 i.u. per g. is also prepared.

**Stilbœstrol**. *Syn.* DIETHYL-STILBÆSTROL.  
 $\text{HO} \cdot \text{C}_6\text{H}_4 \cdot (\text{C}_2\text{H}_5) \cdot \text{C} : \text{C}(\text{C}_2\text{H}_5) \cdot \text{C}_6\text{H}_4 \cdot \text{OH} = 268.3.$

*Dose*.—1 to 5 mg. *per os* or intramuscularly. (1 mg. is equivalent to 40,000 i.u. or 800 i.b.u.).

Stilbœstrol is 4 : 4'-dihydroxy- $\alpha$  :  $\beta$ -diethylstilbene, a derivative of the unsaturated aromatic hydrocarbon stilbene or *trans*-1 : 2-diphenylethylene. It is prepared synthetically and consists of a white, crystalline substance melting at 167° to 168°.

**Insoluble** in water, but soluble in alcohol, most organic solvents and fixed alkali hydroxides; also soluble in oils.

**Uses.** Stilbœstrol acts similarly to the naturally occurring œstrogens. It is highly active by mouth and its duration of action is approximately the same as that of œstradiol. By injection it is said to be about two and a half times as active as œstrone, but is less active than œstradiol benzoate and its action is of shorter duration. It may be employed in all conditions in which the natural hormones are used, and is especially indicated for the relief of the subjective symptoms of the menopause, in atrophic vaginitis, kraurosis vulvæ, pruritus vulvæ and for vulvovaginitis in children. It has also been employed with success for inhibiting lactation. It may occasionally give rise to secondary effects such as nausea and vomiting, but is usually well tolerated.

Stilbœstrol is a comparatively simple substance to synthesise. It imitates the natural œstrogens faithfully and is highly active by mouth.—*Pharm. J.*, i/1939, 31. (For original work see paper by E. C. Dodds, L. Golberg, W. Lawson and L. Robinson, *Nature, Lond.*, i/1938, 247; ii/1938, 34.)

Has an action similar to œstrone on the uterus of ovariectomised rats, on the mating reaction, vagina, and uterus of immature rats, on the uterus of immature rabbits, and on the feathers of capons. By vaginal-smear assay on ovariectomised rats it was found to be approximately  $2\frac{1}{2}$  times as active as œstrone.—E. C. Dodds, W. Lawson and R. L. Noble, *Lancet*, i/1938, 1389.

The duration of action of stilbœstrol is short compared to that of œstradiol benzoate, triphenyl-chlor-ethylene, or œstradiol benzoate butyrate when given subcutaneously. Orally, œstradiol and stilbœstrol act for approximately the same time, and their period of action is a little longer than that of triphenyl-chlor-ethylene.—J. M. Robson, A. Schönberg and Hussein Ahmed Fahim, *Nature, Lond.*, ii/1938, 293.

Diethylstilbœstrol has been found (1) partially to inhibit the response of the pigeon crop-gland to prolactin, (2) to inhibit lactation in the rat, and (3) to produce a temporary increase in the phosphatase content of cows' milk, accompanied by more prolonged increases in both fat and non-fatty solids content. In all these respects its action qualitatively resembles that of natural œstrogens.—S. J. Folley and H. M. S. Watson, *Lancet*, ii/1938, 423.

As active as any known œstrogen, and can be made cheaply. It seems likely to play an important part in therapeutics.—J. H. Gaddum, *Pharm. J.*, i/1939, 28.

In contrast to œstrone, stilbœstrol is only rendered inactive in the organism to a small extent, resembling, in this respect, the hormone esters. Similarly to the hormone esters, stilbœstrol remains deposited at the site of injection for a considerable time (depot formation) and from there it is slowly absorbed. Stilbœstrol is distinguished from the hormone esters by the fact that large amounts are eliminated in the excreta, particularly in the urine.—B. Zondek and F. Sulman, *Nature, Lond.*, ii/1939, 597.

Stilbœstrol, even when given by the mouth, has been shown to produce good results in all the conditions for which œstradiol and œstrone have proved their value, and it has been used with success to induce labour in cases of intra-uterine death of the fetus. The dosage laid down for œstradiol should form the basis of stilbœstrol therapy, but when administered by mouth it is advisable to give it more frequently and in slightly larger quantities. The same principles of treatment should be followed, and it is rarely necessary to give more than 5 mg. daily.—T. N. A. Jeffcoate, *Brit. med. J.*, ii/1939, 676.

**LACTATION.** Lactation was either prevented or inhibited in 20 women by the administration of stilbœstrol 5 to 15 mg. by mouth. In most cases 5 mg. was sufficient.—R. Wenner and K. Joel, *Lancet*, ii/1939, 688.



**VULVOVAGINITIS.** Of 25 cases of gonorrhoeal vulvovaginitis in children ranging from 20 months to 12 years, all were cured by the administration three times daily of a 1 mg. tablet crushed and dissolved in 2 ounces of milk, until a total of 12 tablets had been taken. The rapidity of cure, the absence of toxic or deleterious effects, and the ease of administration renders it an ideal drug for the treatment of vulvovaginitis.—J. D. Russ and C. G. Collins, *J. Amer. med. Ass.*, i/1940, 2446.

**Implantation of Tablets.** Subcutaneous implantation of hard pellets weighing about 100 mg. will give slow absorption with continuous mild oestrus effect. The material seems to be more effective per milligramme absorbed by implantation than by injection or mouth. These small "artificial ovaries" may be left in place for weeks or months, in cases of hypo-ovarianism, without any untoward local effects.—C. M. MacBryde, *J. Amer. med. Ass.*, i/1940, 686.

**Toxic Effects.** Headache and retching in two cases following administration of 1 mg. twice daily.—F. Sanders, *Brit. med. J.*, i/1939, 693.

Though less active than oestradiol benzoate parenterally, stilboestrol is more efficient than the natural oestrogens by mouth, though it is less active than ethinyl oestradiol by mouth. The oral oestrogenic unit for the human being lies between 2 and 4 mg. It is capable of relieving the subjective symptoms of the menopause. In a series of 44 cases treated, its use was associated in 35 with toxic symptoms, including nausea, vomiting, abdominal distress, anorexia, diarrhoea, lassitude, paraesthesia, vertigo, thirst, an acute psychotic reaction and cutaneous rashes. Until the nature of the side-effects of stilboestrol are understood, its use in the human being should be confined to experimental studies.—E. Shorr *et al.*, *J. Amer. med. Ass.*, ii/1939, 2312. (These conclusions as to toxic symptoms were not substantiated by C. L. Buxton and E. T. Engle, *ibid.*, 2318, or by C. M. MacBryde *et al.*, *ibid.*, 2320.)

**The tumorigenic action of stilboestrol** is much greater than that of the natural hormones (oestradiol and oestrone) when equal quantities are compared. The tumorigenic action of small doses is less than that of similar doses of esterified oestradiol, but with greater doses it equals that of similar doses of certain esters of oestradiol (monobenzoate and dipropionate). The guinea-pig uterus increases beyond the normal weight more rapidly with stilboestrol than with free natural hormones. Loss of blood from the genital tract in the guinea-pig treated with stilboestrol is commoner than with the natural hormones, but as common as with similar quantities of the esterified hormones. This is considered to be a sign of greater toxicity of stilboestrol as compared with the natural hormones.—A. Lipschütz and Luis Vargas, *Lancet*, i/1940, 541.

### Stilboestrol Dipropionate.

$C_2H_5 \cdot COOC_6H_4(C_2H_5)C : C(C_2H_5)C_6H_4OOC \cdot C_2H_5 = 380.5$ .

**Dose.**—1 to 5 mg. intramuscularly.

A colourless, crystalline substance obtained by the action of propionic anhydride on stilboestrol. M.p. 104°.

**Uses.** Used for parenteral therapy in preference to stilboestrol itself, since it is believed to liberate stilboestrol slowly, thus giving a prolonged action.

Esterification reduces the activity of diethylstilboestrol, but prolongs the effect. It would appear that the maximum prolongation without undue reduction resides in the dipropionate.—E. C. Dodds, L. Golberg, W. Lawson and R. Robinson, *Nature, Lond.*, ii/1938, 211.

Stilboestrol dipropionate and hexoestrol have oestrogenic properties similar to those of stilboestrol in so far as they are capable of the following actions: (1) inducing uterine haemorrhage in cases of amenorrhoea; (2) relieving the symptoms of the menopausal syndrome; (3) leading to the appearance of cornified cells in the vaginal smear in menopausal cases; (4) restoring the normal conditions of the vulva and vagina in senile atrophic vaginitis; (5) relieving the pain of dysmenorrhoea; (6) inhibiting lactation. Toxic effects, though not severe, developed in 21.6% of cases treated with stilboestrol dipropionate, and in 4.5% of cases treated with hexoestrol.—P. M. F. Bishop *et al.* (Clinical report to the Therapeutic Trials Committee of the M.R.C.), *Lancet*, i/1940, 630.

**Clinestrol** (*Glaxo Laboratories, London*). Tablets containing 0.5, 1 or 5 mg. of stilbœstrol; ampoules containing 1 or 5 mg. of the dipropionate.

**Neo-Oestrano I** (*Crookes Laboratories, London*). Tablets containing 1 or 5 mg. of stilbœstrol; ampoules containing 1 or 5 mg. of the dipropionate.

**Ovodosyn** (*Menley & James, London*). Tablets each containing stilbœstrol 0.5 mg., calcium phosphate 227 mg.

**Pabestrol** (*Paines & Byrne, London*). Stilbœstrol supplied in tablets containing 0.1, 0.5, 1 or 5 mg.; ampoules contain 1 or 5 mg. in solution. Pabestrol D is stilbœstrol dipropionate supplied in the same forms.

**Stilbœstroform** (*British Drug Houses, London*). Brand of diethylstilbœstrol available in ampoules containing 1 or 5 mg. per ml. of oily solution for intramuscular injection and in tablets of 0.5, 1 and 5 mg. for oral administration.

**Syntestrin** (*Richter, London*). Tablets containing 0.5, 1 or 5 mg. of stilbœstrol; ampoules containing 1 or 5 mg. of the dipropionate. Also supplied as an ointment containing 15 mg. of stilbœstrol per oz.

**Hexœstrol**. *Prop. Name.* SYNTHOVO (*Boots, Nottingham*).  $\text{HO}\cdot\text{C}_6\text{H}_4(\text{C}_2\text{H}_5)\text{CH}\cdot\text{CH}(\text{C}_2\text{H}_5)\text{C}_6\text{H}_4\cdot\text{OH} = 270.3$ .

*Dose.*—1 to 5 mg. *per os* three times daily or the same dose intramuscularly.

Hexœstrol is *p*:*p'*-dihydroxy-3:4-diphenyl-*n*-hexane, obtained by the hydrogenation of stilbœstrol in the presence of palladium, or from anethole. It is a white powder melting at 185°.

**Soluble** in alcohol.

**Uses.** Hexœstrol may be used in all conditions in which the natural or synthetic œstrogenic hormones have been employed, and in particular in the symptomatic treatment of the menopausal syndrome, in atrophic conditions of the vagina, for inducing uterine hæmorrhage in amenorrhœa, for the relief of pain in dysmenorrhœa, and for inhibiting lactation. It is slightly less active than stilbœstrol or stilbœstrol dipropionate when given by the mouth, but is more active by injection. It is stated, however, to be less toxic than either of these, and toxic symptoms are rare in dosage up to 2 mg.

### **Triphenylchlorethylene.**

$(\text{C}_6\text{H}_5)_2\text{C}:\text{C}(\text{C}_6\text{H}_5)\text{Cl} = 290.8$ .

A synthetic substance which simulates the action of œstrogenic hormones. It can be safely administered by mouth, by injection or by local application. It causes the same effects as the naturally occurring œstrogens—namely, uterine growth, proliferation of the endometrium, withdrawal bleeding, transition of menopausal to œstrous vaginal smear, relief of menopausal symptoms and inhibition of lactation.

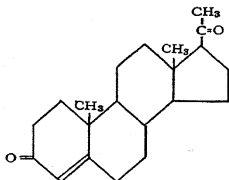
Its action is not sudden or dramatic; it has no definite toxic effects and it can be administered in large doses or over a long period of time; under these conditions adequate dosage is easy to maintain and gives remarkable certainty of action. The duration of action by mouth closely approximates to that of stilbœstrol. By injection, however, the duration is singularly prolonged. The substance is prepared for oral use in tablet form, each tablet containing 200 mg., in ampoules containing 250 mg. dissolved in 5 ml. of sesame oil, for injection, and in vaginal suppositories containing 100 mg. Tablets are given after meals and as many as 9 a day may be given. Two injections are given a week apart to begin with, followed by a third injection three weeks after the second and subsequent injections at intervals of three or four weeks. The suppositories are used

nightly for the first 14 days, and then on every second or third night.—A. I. S. Macpherson and E. M. Robertson, *Lancet*, ii/1939, 1362.

**Progesterone.** *Syn.* HORMONUM LUTEALE (*Fr. Cx.*), PROGESTIN, PREGNENEDIONE.  $C_{21}H_{30}O_2 = 314.45$ .

*Dose.*—1 to 10 mg. (1 to 10 i.u.) daily by intramuscular injection.

Progesterone, pregnene-3,20-dione, is the hormone of the corpus luteum. It can exist in two isomeric forms,  $\alpha$ -progesterone which forms rhombic crystals melting at  $128^\circ$  and  $\beta$ -progesterone which forms mono-clinic needles melting at about  $121^\circ$ .



Progesterone is usually obtained artificially from stigmasterol, a sterol found in soya beans, by chemical degradation, since the supply of corpora lutea is strictly limited. It is excreted in the urine of pregnant women in the inactive form of pregnanediol.

Very **soluble** in alcohol, ether and chloroform, slightly soluble in light petroleum.

Progesterone is standardised biologically according to its effect in causing proliferation of the lining membrane of the uterus in immature rabbits previously sensitised by injections of oestrone. The *international unit* is defined as the amount of progestational activity present in 1 mg. of the standard sample of progesterone.

**Uses.** Progesterone is the hormone which is responsible for transforming the endometrium from the proliferative phase to the pre-gravid phase essential to prepare the uterus for the reception of the fertilised ovum, and it plays an important role in the formation of the placenta and the nutrition of the embryo. It is also stated to inhibit the contractility of the uterus and to be responsible for the further development of the breasts initiated by the follicular hormone. Progesterone only acts on tissues which have been previously subjected to the action of the follicular hormone. Preparations of progesterone are administered by intramuscular injection in the form of an oily solution. Orally, they are without effect.

The principal application of progesterone is in threatened and habitual abortion. In the former, intensive treatment of 5 to 10 mg. daily is advisable until all threatening symptoms have abated;

in the latter, from 1 to 2 mg. twice weekly until the 32nd week, or 1 mg. daily for two months, commencing a month before the usual time of abortion. Progesterone is also of value in certain menstrual disorders, and in particular in the type of functional bleeding known as metropathia hæmorrhagica, which occurs especially in young patients about the age of puberty, and which is successfully treated by the injection of 1 to 5 mg. daily for 5 or 6 days. In amenorrhœa of endocrine origin a course of 5 daily injections of 1 to 5 mg. of progesterone following a previous course of follicular hormone therapy is a rational and successful procedure. The use of progesterone has also been advocated in spasmodic dysmenorrhœa and in pre-eclamptic toxæmia, but the results are doubtful.

Animal experiments strongly suggest that progesterone exerts an *antitumorigenic action*. The quantity necessary to suppress completely the tumorigenic action of oestradiol benzoate is more than 150 times greater than that of the latter. There is support for the hypothesis that the development of uterine fibromyomas in women is due to a disturbance of the normal balance between follicular and luteal hormones and of their normal timing, and that progesterone may prove useful as a therapeutic agent against fibromyoma.—A. Lipschütz, *Lancet*, ii/1939, 420.

**DYSMENORRHŒA.** Divided or single doses of  $\frac{3}{8}$  to 1 rabbit unit given 3 to 6 days before onset of menstruation gave complete relief in 47% of cases, partial relief in 11.7% and failed in 41.3%.—C. A. Elden and K. M. Wilson, *Amer. J. Obstet. Gynec.*, ii/1936, 91.

**Solutum Hormoni Lutealis** (*Fr. Cx.*) is a solution of progesterone for injection containing 1 mg. of progesterone per ml. of sterilised neutral olive oil.

**Extractum Corporis Lutei Depuratum** (*Fr. Cx.*). An extract of fresh corpora lutea containing progesterone but freed from œstrone.

**Solutum Extracti Corporis Lutei Depurati** (*Fr. Cx.*). A solution of purified extract of corpora lutea in sterilised neutral olive oil for injection. It should have the same specific gravity as Solutum Hormoni Lutealis (*Fr. Cx.*).

**Colutamin** (*Richter, London*). Water-soluble preparation of corpus luteum. *Dose*.—1 ml. by injection daily or 2 to 3 tablets thrice daily. In amenorrhœa and sexual deficiency.

**Colutoid** (*Richter, London*). Lipoids of corpus luteum. *Dose*.—1 ml. intramuscularly daily, or 1 to 2 tablets thrice daily. In menorrhagia, dysmenorrhœa, etc.

**Gestone** (*Paines & Byrne, London*). 1 ml. ampoules of progesterone in oily solution containing 1, 2, 5 or 10 i.u.

**Glanducorpin** (*Richter, London*).  $\frac{1}{2}$  and 1 ml. ampoules of progesterone containing 2 i.u. per ml. Also 1 ml. ampoules containing 5 i.u. per ml.

**Lipo-Lutin** (*Parke, Davis, London*). A standardised oil solution of progesterone issued in 1 ml. ampoules containing 1 rabbit unit.

**Luteostab** (*Boots, Nottingham*). An oil solution of progesterone containing 2 rabbit units per ml.

**Lutocyclin Ampoules** (*Ciba, Horsham*). 1 ml. ampoules of progesterone containing 2, 5 or 10 mg.

**Eutogyl Ampoules** (*Roussel Laboratories, London*). 1 ml. ampoules of an oil solution of progesterone containing 2, 5 or 10 mg. per ml.

**Lutren** (*Bayer Products, London*). 1 ml. ampoules of an oil solution of progesterone containing 2 or 5 i.u.

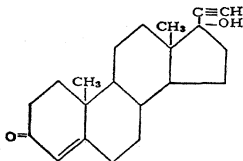
**Progestone** (*Carmick, Newark, N.J.; Brooks & Warburton, London*). 1 ml. ampoules of progesterone in oil containing  $\frac{1}{2}$ ,  $\frac{1}{4}$ ,  $\frac{1}{2}$ , 1 or 5 i.u.

**Proluton Ampoules** (*Schering, London*). 1 ml. ampoules of progesterone in oil containing 2, 5 or 10 mg.

**Pregneninolone.** *Syn.* PREGNENINONOL, ANHYDRO-HYDROXY-PROGESTERONE, ETHINYL TESTOSTERONE.  $C_{21}H_{28}O_2 = 312.4$ .

*Dose.*—10 to 60 mg. by the mouth.

A white, crystalline substance melting at  $269^\circ$  to  $272^\circ$ .



**Insoluble** in water, but soluble in dioxane.

A modification of progesterone synthesised by Inhoffen and Hohlweg, and possessing marked progestational activity when administered by the mouth, the effective dose being six times the effective dose of progesterone given by intramuscular injection.

It has been successfully employed in amenorrhœa, dysmenorrhœa, menorrhagia, metropathia hæmorrhagica, and in threatened and habitual abortion.

In normally menstruating women, uterine hæmorrhage has been induced during the intermenstrual stage by giving pregneninolone *per os* in the post-menstruum. In secondary amenorrhœa, hæmorrhage has been induced by oral administration of pregneninolone without preliminary treatment with oestrogenic hormone. The effective dose of pregneninolone given by mouth is about six times greater than the effective dose of progesterone given by intramuscular injection.—B. Zondek and S. Rozin, *Lancet*, 1/1939, 504; see also *ibid.*, 519.

**Lutocyclin Oral** (*Ciba, Horsham*). Tablets each containing 5 mg. of pregneninolone.

**Lutogyl Tablets** (*Roussel Laboratories, London*). Each tablet contains 5 mg. of pregneninolone.

**Proluton C** (*Schering, London*). Dragées each containing 5 or 10 mg. of pregneninolone.

**Progestoral** (*Organon Laboratories, London*). Tablets each containing 5 or 10 mg. of pregneninolone.

#### PROPRIETARY OVARIAN GLAND PRODUCTS

**Agomensin** (*Ciba, Horsham*). Water-soluble ovarian substance. *Dose.*—1 to 3 tablets three times a day or 1 to 4 ampoules, subcutaneously or intramuscularly, 2 or 3 times a week. In functional amenorrhœa.

[P1] **Climatone** (*Paines & Byrne, London*). Tablets containing the full hormone complement of ovary whole gland, with theobromine-calcium, calcium lactate, nitroglycerin and menthyl valerianate. *Dose.*—1 or 2 three times daily before meals for 4 weeks, repeated after an interval of one week. Menopausal hypertension, flushing, etc.

**Crinex** (*Continental Laboratories, London*). Standardised ovarian extract. Supplied as ampoules, tablets and drops.

**Glanduovin** (*Richter, London*). Extract of whole ovarian gland. In ampoules of two strengths for intramuscular or subcutaneous administration.

**Gynocalcion M** (*Anglo-French Drug Co., London*). A combination of calcium acetate, with manganese, phosphorus, and ovarian and orchitic extracts, in the form of dragées. *Dose*.—12 to 16 dragées daily for two periods of 10 days a month separated by an interval of 8 days. In menopausal disorders.

**Hormofort Ovarian** (*Richter, London*). Ovarian gland  $1\frac{1}{2}$  gr., ovarian follicular hormone 100 i.u. *Dose*.—3 tablets daily.

**Lipamensin** (*Paines & Byrne, London*). Fractionated extract of ovarian residue. Tablets or ampoules.

[P1-87] **Matronax** (*Knoll, London*). Ovarian substance  $\frac{1}{2}$  gr., Thyraden  $\frac{1}{16}$  gr., Bromural  $2\frac{1}{2}$  gr., calcium diuretin  $2\frac{1}{2}$  gr. For menopausal disorders.

[P1-87] **Menocrin Tablets** (*Endocrines-Spicer, Watford*). Tablets containing whole ovary with follicular fluid, thyroid, total pituitary, magnesium phosphate, calcium phosphate (dibasic) and glycerophosphate, potassium and sodium bicarbonates. Also supplied in ampoules for injection.

**Ovacliman** (*Richter, London*). Bromised ovary (80% ovary, 20% bromine) 0.05 g., theobromine 0.05 g., calcium lactate 0.2 g., benzyl succinate 0.03 g. *Dose*.—1 or 2 tablets thrice daily.

[P1-87] **Ovacoids** (*Reed & Carnrick, Jersey City; Coates & Cooper, London*). Fresh ovary 5 gr., fresh anterior pituitary  $\frac{1}{2}$  gr. *Dose*.—2 tablets thrice daily.

**Ovamammoid Compound Capsules** (*British Organotherapy Co., London*). contain 1 gr. each of ovarian extract and mammary gland extract. *Dose*.—1 thrice daily  $\frac{1}{2}$  hour before meals and one at bedtime.

**Ovobrol** (*Roche Products, Welwyn Garden City*). Ovarian-bromide preparation in the form of soup cubes, each corresponding to 1 g. of fresh gland and 1 Sedobrol cube (= 17 gr. of sodium bromide).

[P1-87] **Panatox** (*Paines & Byrne, London*). Tablets contain ovary (w.g.)  $\frac{1}{2}$  gr., testis  $\frac{1}{2}$  gr., thyroid  $\frac{1}{16}$  gr., pituitary (w.g.)  $\frac{1}{16}$  gr., suprarenal (w.g.)  $\frac{1}{16}$  gr. *Dose*.—1 to 4 tablets thrice daily. Also supplied as elixir.

[P1-87] **Polyglandin** (*Allen & Hanburys, London*). 5-gr. capsules each containing fresh mixed glands, pituitary  $\frac{1}{2}$  gr., thyroid  $\frac{1}{2}$  gr., ovary  $2\frac{1}{2}$  gr., testes  $2\frac{1}{2}$  gr. *Dose*.—1 or 2 capsules two or three times daily. Also available as an elixir and as a solution for injection.

**Prokliman** (*Ciba, Horsham*). Tablets containing ovarian hormones 0.02 g., Peristaltin 0.015 g., caffeine sodium salicylate 0.05 g., Kryofine 0.2 g. For the treatment of all forms of climacteric disturbances. Kryofine is described as methoxyacet-*p*-phenetidin, a non-toxic phenacetin derivative with antipyretic and antineuralgic properties.

[P1-87] **Thyrovarian Compound Tablets** (*Parke, Davis, London*). Desiccated ovarian substance 3 gr., desiccated suprarenal gland 1 gr., desiccated thyroid gland  $\frac{1}{2}$  gr. *Dose*.—1 tablet twice daily.

**Varium** (*Burroughs Wellcome, London*) is a brand of ovarian substance in 5-gr. tablets.

### The Bi-sexual Properties of the Sex Hormones.

Although the terms "male" and "female" sex hormones are still retained as a legacy of the early work on these substances, recent researches have shown that there is no justification for differentiation such as these terms would imply. It is now known, in fact, that all oestrogens have some androgenic activity and all androgens have some oestrogenic activity; in other words, with few exceptions, bi-sexual property must be considered the common attribute of nearly all the sex hormones. A great deal of work has been conducted on this subject, mostly by Korenchevsky and his associates, and these workers have suggested the following new classification (*Brit. med. J.*, ii/1937, 896) in place of the old classification of "male" and "female" hormones: (i) *Purely male*

or female hormones. So far as is shown by rat experiments, progesterone is the only member of this group, and may be defined as a pure female hormone. (ii) *Partially bi-sexual hormones*:—(a) *Hormones with chiefly male characters*: androsterone, testosterone propionate, androstenediol, and probably  $\Delta^4$ -androstenedione. (b) *Hormones with chiefly female properties*: oestrone and oestradiol belong to this group. (iii) *True bi-sexual hormones*: to this group seem to belong *trans*dehydroandrosterone, testosterone and  $\Delta^4$ -androstenediol, since in prolonged experiments they bring about a return to or towards the normal of all the atrophied sexual organs to approximately the same degree in males and females. Broadly speaking it may be said in respect of this last group that the male benefits by direct action as a result of androgen therapy, and the female benefits indirectly by a counteracting effect on ovarian hyperfunction. While successful results have been reported by numerous workers in the conditions referred to, the methods would appear to be somewhat unreliable, and there is the possibility that the administration of large doses of androgens to females may give rise to unpleasant masculinising side-effects.

The matter is further complicated by the fact that certain of the sex hormones exert a co-operative action when given in the form of combined injections, while in other cases there may be antagonistic action. Thus, as an example of co-operative action, it has been shown that the simultaneous administration of androsterone and oestrone to rats causes a greater increase in the weight of the prostate and seminal vesicles than is caused by androsterone alone; and, as an example of antagonistic action, it is found that when castrated mice are maintained in continuous oestrus by daily injections of oestrone the simultaneous administration of testosterone propionate inhibits oestrus. It is obvious that the complex inter-relationships of the sex hormones are at present but inadequately appreciated, and it is probable that their therapeutic applications will be subject to continuous modification for some time to come.

In female rats testosterone suppresses the appearance of normal oestrus and causes an increase in the size of uterus, vagina and preputial glands, the histological changes produced being reminiscent of those seen in pregnancy. With few exceptions, bi-sexual activity, though weak in some hormones, must be considered to be one of the common properties of nearly all the sexual hormones.—V. Korenchevsky, M. Dennison and K. Hall, *Biochem. J.*, 1937, 780.

A comparison of the efficiency of various preparations of androgens given by different routes in maintaining sexual function in a male post-puberal eunuch. The minimum effective dose of testosterone propionate given by subcutaneous injection was 40 mg. per week; to obtain an equivalent effect it was found necessary to give 2 to 3 times this dose rubbed in as ointment, 6 times the dose rubbed in as tincture, or 20 times the dose by mouth. Progesterone was found to prolong the action of testosterone propionate when given in conjunction with it.—G. L. Foss, *Lancet*, i/1939, 502.

OTOSCLEROSIS. Sex hormones have been administered with beneficial results in otosclerosis. Of 18 males treated 7 were improved and 11 not improved, and of 38 females 24 were improved and 14 not improved. The males generally showed most improvement following the use of the female hormones (oestrone, stilboestrol, etc.), and the females following the use of male hormones (e.g., Perandren—the propionic ester of synthetic androsterone). There is some

intimate connection between the gonadal internal secretions and otosclerosis—it may be that there is an imbalance between the male and female hormones, which can be rectified by administration of the deficient hormone.—J. Bernstein and L. Gillis, *Lancet*, ii/1939, 1368.

## ANDROGENS

The essential action of the hormones of this group, which consists of testosterone and its derivatives, is the promotion of the growth and the maintenance of the size and function of the accessory sexual organs in the male. The first crystalline androgens isolated were androsterone and dehydroandrosterone, which were crystallised from male urine. Soon after they were produced by the synthetic degradation of cholesterol, and considered to be the active testicular secretion although their potency in producing comb-growth in the capon and enlargement of the seminal vesicles and external genitalia of the castrated rat proved to be very low. Subsequently, however, another androgenic substance, testosterone, was separated from bull testis-tissue, and soon after it was prepared artificially from cholesterol and established as the natural hormone of the testes. Androsterone is now considered to be an excretion product of testosterone, and dehydroandrosterone an intermediary product of the synthesis of testosterone within the body. To date, six naturally occurring androgens have been isolated, four of them from human urine, and some sixty androgenic substances have been prepared artificially. Study of the formulæ of androgens, all of which are derivatives of androstane, reveals that the critical points in their formulæ are represented by the carbon atoms 3 and 17, and by the position of the unsaturated linkage.

**Esters.** When testosterone was isolated from the testes by E. Laquens and his collaborators, they pointed out that there was present in testis-tissue an "X" substance which was itself inactive, but had the power of increasing the effectiveness of testosterone. Investigation of this substance suggested that it was not a hormone, but a mixture of fatty acids including palmitic acid, which was found to be present in testis-tissue, and it was shown that an even greater effect could be produced by the esterification of testosterone. Numerous esters were prepared and tested by their actions on the rat prostate and seminal vesicles, and on the capon comb. Of these, testosterone propionate was found to have a particularly favourable effect both in intensity and duration of action.

**Standardisation.** Two methods of standardisation of androgenic activity are in common use, each of them depending on the counteraction of castration effects by the administration of the substance to be tested. The capon-comb test depends upon the increase in size of the capon's comb which the substance causes, and the seminal vesicle test upon the growth of the seminal vesicles and prostate of young castrated rats. In both tests the effects produced are compared with those of the international



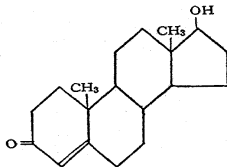
standard preparation of androsterone. The international unit of male hormone activity is defined as the activity of 0.1 mg. of the international standard preparation of androsterone, as measured by a specific biological reaction. It was agreed that all comparisons should be made by the capon-comb method which, although it does not reveal the effects of esterification of testosterone, gives a more exact response weight by weight for androgens, and seems to be a better medium than the seminal vesicle test for a purely quantitative test of total activity.

**Comparisons of activity of the androgens.** On the basis of the effects produced on the seminal vesicles and prostate, Korenchevsky and Dennison (*Biochem. J.*, 1936, **30**, 1514) found one rat unit of male hormone activity to be present in 8 gamma of testosterone, 21 gamma of androstanediol, 170 gamma of androsterone and 940 gamma of dehydroandrosterone, and they also found that in addition to its greater activity testosterone, unlike androsterone, appears to bring about a qualitatively normal development of the male sex organs. These findings are not surprising when it is recalled that testosterone is the actual male sex hormone present in testicular tissue, whereas the other androgens are merely excretion products occurring in male urine.

Subsequently it was found that an even greater effect could be produced by the esterification of testosterone, the increase in the weight of the seminal vesicles of the rat following a single injection of testosterone propionate amounting to 12 times that produced by the same amount of free testosterone. By reason, therefore, of its greater activity and more prolonged action, testosterone propionate is the androgen most frequently employed in clinical practice.

**Testosterone.**  $C_{19}H_{28}O_2 = 288.41$ .

Testosterone,  $\Delta^4$ -androstene-17-*trans*-ol-3-one, the true testicular hormone, is a crystalline substance melting at  $154^\circ$ . It is



obtained from testicular tissue and, artificially, by chemical degradation of the cholesterol molecule.

**Insoluble** in water but soluble in organic solvents.

Testosterone has been successfully employed by inunction in the treatment of hypogonadism, but it is now more usual to employ the propionate owing to its greater activity.

Testosterone or testosterone propionate applied on the skin as an ointment is readily absorbed and either maintains the accessory reproductive organs of castrate males in a normal reproductive state or stimulates their development precociously in the young or decidedly above the normal level in adults. These androgens, so administered, exert effects similar to those following subcutaneous injections.—C. R. Moore *et al.*, *J. Amer. med. Ass.*, ii/1938, 11.

In castrated patients and in those with hypogonadism due to cryptorchidism the administration of testosterone brings about an effective substitution. Beneficial results have been obtained through the intramuscular injection of testosterone propionate and equally good results through the inunction method with free testosterone in a greaseless base.—W. M. Kearns, *J. Amer. med. Ass.*, i/1939, 2255.

**Testosterone Propionate.**  $C_{19}H_{27}O_2 \cdot CO \cdot C_2H_5 = 344.5$ .

*Dose.*—5 to 25 mg. daily by intramuscular injection or by inunction.

Testosterone propionate is the ester of testosterone and propionic acid. It is a crystalline substance melting at  $123^\circ$  and soluble in oils.

*Uses.* The androgens are chiefly employed in males as substitution therapy whenever the organism is incapable of secreting an adequate amount of the testicular hormone, and they are responsible for the development of the male secondary sex characters. Their employment is therefore indicated in conditions resulting from the arrest or retardation of puberty, as in eunuchoidism and hypogonadism, in impotence especially when associated with endocrine insufficiency, in cryptorchidism, in surgical castration and in prostatic hypertrophy. In all cases it should be borne in mind that androgen therapy is pure substitution therapy and that to obtain a permanent result a maintenance dose will be required.

The androgens may also be employed in the treatment of certain conditions in the female such as menorrhagia, dysmenorrhœa, mastodynia and chronic mastitis.

Owing to its much greater activity, testosterone propionate is now employed almost to the exclusion of the other androgens. It is usually given by intramuscular injection in oil, in a dose of from 10 to 25 mg. daily or every other day, and in a dose of 5 mg. every other day in females. It is also effective when employed by percutaneous administration in the form of ointment. According to Foss (*Lancet*, ii/1939, 502), a comparison of the efficacy of testosterone propionate by various routes shows that, as compared with subcutaneous injection, the dose by inunction of ointment must be two to three times as great, by inunction of solution in spirit six times as great, and by mouth twenty times as great. More recently it has been successfully employed by the subcutaneous implantation of tablets, the amounts implanted varying from 300 to 1600 mg. Testosterone propionate should not be given in high doses in the presence of hypertension.

The effects of testosterone on castrated rats are increased by the addition of fatty acids, the increase being very great with normal saturated acids having sixteen C atoms. The testosterone esters most effective in promoting growth of

the capon's comb are those of the lower fatty acids. In rats maximum intensity and duration is obtained, among the lower fatty acids, with the esters of propionic acid.—K. Miescher, A. Wettstein and E. Tschopp, *Biochem. J.*, 1936, 1970.

The administration of 25 mg. of testosterone propionate twice weekly to normal mature female rhesus monkeys stopped the menstrual cycle during the period of injections. The internal reproductive organs are not injured by the treatment. Follicular growth and luteinisation are both inhibited. It is suggested that testosterone propionate may be of clinical value for the induction of temporary sterility and the control of uterine bleeding.—S. Zuckerman, *Lancet*, ii/1937, 676.

**Antitumorigenic action.** When the monobenzoate ester of oestradiol was given to castrated guinea-pigs simultaneously with testosterone propionate, up to the proportion of 1 : 13, uterine and extra-uterine fibroids developed in the usual manner, as with similar quantities of the ester of oestradiol alone. When the proportion of oestradiol to testosterone was raised to 1 : 22 or more, no fibroids of appreciable size developed.—A. Lipschütz, L. Vargas and O. Ruz, *Lancet*, ii/1939, 867.

**EUNUCHOIDISM.** Percutaneous application in a fatty vehicle effective in the treatment of eunuchoidism, though a larger dose is required than when the hormone is given by injection. An ointment containing 25 mg. of testosterone propionate per gramme in a 2 gramme collapsible tube is recommended for practical use.—G. L. Foss, *Lancet*, ii/1938, 1284.

**INHIBITION OF LACTATION.** Excellent results in 19 out of 21 cases from deep intramuscular injection of 25 mg. twice daily for one or more days. Complete relief of all symptoms was usually obtained within a few hours after the second dose (eight hours after the first dose). There was no tendency to recurrence of symptoms after injections were stopped and there were no unpleasant side effects.—R. Kurzrok and C. P. O'Connell, *Endocrinology*, 1938, 23, 476.

Favourable results in 49 out of 56 patients. The results were uniformly good with a total dosage of 125 or 150 mg. given in divided doses of 25 to 50 mg. intramuscularly at 12 hour intervals. Lactation, engorgement and pains in the breasts did not recur after treatment was stopped. Single doses of 100 and 125 mg. were generally ineffective regardless of the time of administration.—C. H. Birnberg, *Amer. J. Obstet. Gynec.*, 1940, 107.

50 patients treated with total doses varying from 25 to 125 mg. in three or four divided doses every 12 hours with successful results in 47. As little as 10 mg. doses appeared to be as effective as larger doses.—S. L. Siegler and L. M. Silverstein, *ibid*, 109.

**MASTITIS.** Mammary pain was relieved in every one of 8 patients with chronic mastitis by the daily inunction of the breast with an ointment of testosterone propionate containing 3 to 10 mg. of active substance. No undesirable side-effects were observed.—A. W. Spence, *Lancet*, ii/1940, 387.

Androgens can alleviate the symptoms of most cases of chronic mastitis, but the beneficial effect is not permanent, and undesirable effects may rob the treatment of its value. In one case carcinoma of the breast developed ten months after a course of testosterone propionate injections. The histological changes produced by androgens up to the limit of tolerance are insignificant.—H. J. B. Atkins, *Lancet*, ii/1940, 412.

**MENTAL DISORDERS.** Four cases of severe mental disorder in men successfully treated with testosterone propionate (Testoviron) or androsterone benzoate (Proviron).—A. Guirrdam, *Brit. med. J.*, i/1940, 10.

**METRRORRHAGIA and menorrhagia** can as a rule be controlled by injection of testosterone propionate in adequate doses. The amounts required depend on the clinical findings and the pathology of the condition. A temporary therapeutic menopause with its associated symptoms can be induced with large doses. Menstruation may be postponed for several months after treatment; ovulation and luteinisation can be inhibited, and the endometrium is usually found to be in the resting stage. The breasts become smaller. No harmful effect has been noticed in 16 patients treated during 9 months, with total doses up to 2200 mg.—G. L. Foss, *Lancet*, i/1938, 992.

Male hormone was implanted subcutaneously to control serious menorrhagia caused by fibroids. Good results were obtained in the case of women near the menopause. The dose employed varied from 300 to 1600 mg. in tablets, each containing 50 mg. All the patients experienced an increased sexual drive and a great feeling of general well-being.—A. A. Loeser, *Brit. med. J.*, i/1940, 481.

**PROSTATIC HYPERTROPHY.** Twenty-seven out of 34 cases of prostatic hypertrophy treated with testosterone propionate in oily solution responded well—frequency of micturition decreased, emission of urine was easier, and urgency and the burning sensation disappeared. Decrease of vesical residuum was obtained in some patients suffering from partial retention, and in some the symptom completely disappeared. One notable effect was the reduction in blood pressure. No definite decrease in the volume of the prostate was noted, although the swelling was arrested. The dosage used was 5 to 10 mg. (250 i.u.) daily by intramuscular injection, or 20 mg. every four days. On an average, some diminution of symptoms was obtained in 10 to 12 days; a decided improvement must be recorded before cessation of the injections, and they may then be suspended until recurrence is noted—an average of from three to six months, or even one year.—A. Aberholtzer, *Brit. J. Urol.*, 1938, 10, 237.

**Methyl Testosterone.** Methyl testosterone is very efficacious by mouth, being about twice as active as testosterone by this route. Potency was fully maintained in a eunuch with 100 mg. daily and a lower dosage of 50 mg. is effective. All the signs of puberty can be rapidly produced in cases of genital hypoplasia affecting not only sexual but physical development, and for such patients it is probable that much smaller doses would be adequate. Oral therapy with this androgen may ultimately replace all other methods of using testosterone or its propionate.—G. L. Foss, *Brit. med. J.*, ii/1939, 11.

**Neo-Hombreol** (*Organon Laboratories, London*). 1 ml. ampoules of testosterone propionate in oil containing 5, 10 or 25 mg. Also available as an ointment containing 2 or 25 mg. per g.

**Perandren** (*Ciba, Horsham*). 1 ml. ampoules of testosterone propionate containing 5, 10 or 25 mg. Also available as an ointment containing 2 mg. per g.

**Sterandryl** (*Roussel Laboratories, London*). 1 ml. ampoules of testosterone propionate in oil containing 5, 10 or 25 mg. **Ecto-Sterandryl** is a solution of testosterone in oleic alcohol containing 50 mg. per 10 ml. For percutaneous administration.

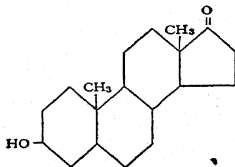
**Testoviron** (*Schering, London*). 1 ml. ampoules of testosterone propionate in oil containing 5, 10 or 25 mg. Also supplied as an ointment containing 10 mg. of testosterone per g.

**Virormone** (*Paines & Byrne, London*). 1 ml. ampoules of testosterone in oil containing 2 or 5 mg.

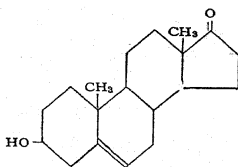
**Androsterone.**  $C_{19}H_{30}O_2 = 290.4$ .

Androsterone, androstane-3-*cis*-ol-17-one, is an excretion product of testosterone obtained from male urine and, artificially, by chemical degradation of the cholesterol molecule. It is a crystalline substance melting at 178°.

**Insoluble** in water but soluble in organic solvents and oils.



Androsterone.



Dehydroandrosterone.

**Dehydroandrosterone.** *Syn.* TRANSDEHYDROANDROSTERONE.  $C_{19}H_{28}O_2 = 288.4$ .

Dehydroandrosterone,  $\Delta^4$ -androsterene-3-*trans*-ol-17-one, is a

crystalline substance obtained from male urine and, artificially, by the chemical degradation of the cholesterol molecule. It melts at 148° and is soluble in oil.

**Androfort** (*Richter, London*). A preparation for intramuscular injection containing 2 i.u. androsterone per ml. in oily solution. For sexual debility, impotence, prostatic enlargement.

**Hombreol** (*Organon Laboratories, London*). 1 ml. ampoules containing 4 or 20 i.u. of androsterone.

**Proviron** (*Schering, London*). 1 ml. ampoules containing 5 mg. of androsterone benzoate in oil solution for intramuscular injection.

### PROPRIETARY MALE GLAND PRODUCTS.

**Androstin** (*Ciba, Horsham*). Ampoules A and B containing respectively the hydrosoluble and liposoluble principles of the gland. One ampoule A and one ampoule B together represent 16 g. of fresh gland. Tablets are also available equivalent to 8 g. of fresh gland.

**Erugon** (*Bayer Products, London*). Whole testicular extract in oily solution for intramuscular injection. Each ampoule contains 2 cock's comb growth units. Also available in pellets containing  $\frac{1}{2}$  unit.

**Gynofort** (*Richter, London*). Tablets containing testis 0.2 g. and seminal vesicle 0.02 g. *Dose*.—1 to 3 tablets thrice daily. In frigidity.

[P1-S1-S7] **Homovir** (*Anglo-French Drug Co., London*). Tablets containing thyroid 0.005 g., suprarenal 0.016 g., pituitary (whole) 0.03 g., prostate 0.03 g., orchis 0.06 g., yohimbine 0.002 g. Also available in ampoules for injection.

[P1-S1] **Orkitone** (*Anglo-French Drug Co., London*). An elixir containing fresh orchitic gland 21.25 g., nucleinic acid 0.326 g., disodium methylarsenate 0.05 g., sodium glycerophosphate 50% 0.5 g., saccharated hydro-alcoholic solution to 100 g. *Dose*.—1 tablespoonful thrice daily.

[P1-S1] **Prostatin** (*Paines & Byrne, London*). Prostate, testis, and cerebrin, of each 15 gr. of fresh gland, yohimbine hydrochloride  $\frac{1}{8}$  gr., in ampoules of 1 ml.

[P1-S1] **Protestin** (*Richter, London*). Brain, prostate, testis and yohimbine. Tablets and ampoules.

**Testacoids** (*Reed & Carnrick, Jersey City; Coates & Cooper, London*). Tablets representing fresh testicle 25 gr., fresh prostate 5 gr. *Dose*.—3 tablets thrice daily. Male hypofunction.

**Testanon** (*Organon Laboratories, London*). Dried total testes in tablets.

[P1-S7] **Thyorchic Compound Tablets** (*Parke, Davis, London*). Desiccated orchitic substance 3 gr., desiccated suprarenal gland 1 gr., and desiccated thyroid gland  $\frac{1}{2}$  gr. *Dose*.—1 tablet before meals.

[P1] **Tonicine** (*Reed & Carnrick, Jersey City; Coates & Cooper, London*). Liquid gonadal tonic. 1 dr. = fresh testicle 25 gr., strychnine sulphate  $\frac{1}{320}$  gr., sodium glycerophosphate 1 gr.

## OLEA ESSENTIALIA

Taken internally, the volatile oils exert a mild irritant action on the mucous membrane of the mouth and the digestive tract, which induces a feeling of warmth and increases salivation, and for this purpose they are included in stomachic mixtures to stimulate appetite and aid digestion. During excretion they stimulate the secretions of the bronchial glands and act as mild expectorants. The irritant action also causes some acceleration of respiration, stimulation of the heart's action and a transient rise of blood pressure, and they are therefore employed as reflex restoratives in syncope, though usually in conjunction with more potent

irritants, *e.g.*, aromatic spirit of ammonia. Taken after meals they are carminative and are employed for the relief of gastric discomfort and of flatulent colic, as also to counteract the griping tendencies of purgatives.

All the volatile oils are antiseptics, and when taken internally they check the growth of fermentative organisms in the stomach; their antiseptic properties are also made use of in the preparation of tooth pastes and powders, their stimulant and rubefacient action on the gums being a further advantage in this connection. Owing to their irritation of the renal epithelium, many of the volatile oils promote diuresis, and after excretion they act as urinary antiseptics, *e.g.*, oil of sandalwood and oil of copaiba.

When applied to the intact skin they have an irritant and rubefacient action, causing first a sensation of warmth and smarting, which is later replaced by a mild local anæsthesia. For this reason they are much used as counter-irritants and cutaneous stimulants in the treatment of chronic inflammatory conditions, to relieve neuralgia and rheumatic pains, and for application to the chest wall in bronchitis, pleurisy, etc.

When inhaled they arrest profuse secretion and relieve congestion of the bronchioles, and they may be employed for this purpose, and for their mild antiseptic action, in conditions such as chronic bronchitis.

Notes on essential oils and their preparations not included in the following group are given under the drugs from which they are manufactured (*see* Index).

Solutions of essential oils containing no alcohol may be made by the use of soaps, the solutions remaining transparent on dilution with water to any extent. As an example, oil of citronella 25 ml., is mixed with strong solution of ammonia 8.5 ml., and ammonium "ricinoleosulphate" soap solution added to produce 100 ml., care being taken that no globule of oil escapes the action of the soap. The solution of ammonium ricinoleo-sulphate is made by the action of sulphuric acid on castor oil below 30° and, after purification, it is diluted so as to contain 50% of solids. A table of essential oils, auxiliary and soaps is given.—A. Albert, *J. Soc. chem. Ind., Lond.*, 1939, 58, 196.

**Oleum Bergamottæ** (B.P.C., *Fr. Cx.*, *P. Jap. V*). *Syn.* ESSENCE OF BERGAMOT. Expressed from the fresh peel of the fruit of *Citrus Aurantium* subsp. *bergamia*, and largely employed in perfumery, especially in preparations for the hair.

**Spiritus Coloniensis** (B.P.C.). *Syn.* AQUA COLONIENSIS. A form of eau de Cologne containing oil of bergamot for use in hair lotions, etc.

**Eau de Cologne** (*Fr. Cx.*). *Syn.* TEINTURE D'ESSENCE CITRON COMPOSÉE. One litre contains oils of bergamot, orange and lemon 10 g., oils of orange-flower and rosemary 2 g., in alcohol 90%.

**Oleum Cajuputi** (B.P., *P. Helv. V*).

*Dose.*—1 to 3 minims (0.06 to 0.2 ml.).

Distilled from the fresh leaves and twigs of *Melaleuca Leucadendron* and other species of *Melaleuca* (Myrtaceæ) and redistilled in steam. Contains 50 to 65% of cineole,  $C_{10}H_{18}O$ .

It has the typical actions of a volatile oil, and is employed internally as a carminative, and externally as a counter-irritant in rheumatism.

**Spiritus Cajuputi (B.P.).**

*Dose.*—5 to 30 minims (0.3 to 2 ml.). 1 in 10.

**Leucadol.** A redistilled oil of cajuput boiling below 235°, fractionated from the high-boiling constituents. A yellow liquid, sp. gr. 0.922, cineole content 78%. Has been employed in chest affections by injecting into the bronchi. It is miscible with iodised oil in all proportions, with which it has been used for diagnosis. Mix with olive oil up to 5% for oleothorax, or weaker for intratracheal injection.

**Oleum Cedri (B.P.C.).** *Syn.* OIL OF RED CEDAR, CEDRI LIGNI OLEUM. Chiefly from *Juniperus virginiana* (Pinaceæ), also from chip shavings and sawdust of pencil cedar (*J. americana* and *J. bermudiana*). It yields a stearoptene, cedrene camphor (cedrol),  $C_{15}H_{26}O$ , and the sesquiterpene cedrene,  $C_{15}H_{24}$ , the odour of which is distinct and stronger than the camphor, and taste finally peppery. Oil largely used in perfumery, also, in a thickened form by concentration *in vacuo* and admixture with other substances, in microscopical work with oil immersion lenses. It has also been used internally in the treatment of gonorrhœa, but is of doubtful value.

The oil from *Cedrus atlantica*, *Syn.* LIBANOL, has been given in 8-m. capsules, in doses of up to 6 per diem, in phthisis, bronchitis and skin affections. A 25% ointment in soft paraffin has also been used in skin affections.

**Urocedrol** (*Anglo-French Drug Co., London*). Essential oil of *Cedrus atlantica*, with hexamine camphorate and salol. *Dose.*—6 to 10 capsules daily. Gonorrhœa, cystitis, pyelitis, etc.

**Oleum Citronellæ (B.P.C., P. Helv. V).** Obtained from *Cymbopogon Nardus*. Ceylon oil contains not more than 10% of citronellal; Java oil (including oil from Burma and the Straits Settlements) contains from 30 to 40%. Used as a perfume for soap and as an insect repellant.

The old "Bamber Oil" used in India has now been replaced in the Army by an anti-mosquito cream with the following formula: oil of citronella 18.25%, camphor 1%, cedarwood oil 1%, hard paraffin 17.25%, soft white paraffin 45%. Applied to hands, face, neck and ears it will keep off mosquitoes for 6 hours, and is an excellent protection against sandflies. It is now used in India, Egypt and Palestine.—J. A. Manifold, *Trans. R. Soc. trop. Med. Hyg.*, 1939, 33, 298.

**Oleum Eucalypti (B.P., U.S.P. XI, Fr. Cx., P. Helv. V).**

*Dose.*—1 to 3 minims (0.06 to 0.2 ml.) on sugar, emulsified, or mixed with olive oil. *U.S.P. XI average dose* 8 minims.

Eucalyptus oil is distilled from the leaves of numerous species of *Eucalyptus*. The oils which contain a large percentage of eucalyptol and little phellandrene are used chiefly for pharmaceutical purposes. The most important species now being distilled for oils of this class are *E. polybractea* and *E. dumosa*. Unmixed oil of *E. globulus* is no longer an article of commerce. As the yield of oil varies greatly with the several species this is a controlling factor. The rectified oils of *E. polybractea* and *E. Australiana* are water white; some oils are tinged slightly yellow when freshly distilled. The oil from *E. citriodora* has an odour resembling that of lemon-grass.

**Soluble** in oils, fats, paraffins, about 3 in 1 of alcohol 90%, in about 3 to 5 vols. of alcohol 70% and in all proportions in absolute alcohol.

**Toxic Effects.** Poisoning effects from 1 to 6 drachms are recorded. Effects were gastro-intestinal irritation and cerebral paresis with vomiting and diarrhoea. Treatment by external stimulation, as on the lines of opium poisoning.

Eucalyptus and castor oil taken in error for plain castor oil. Three doses of camphor given hypodermically. Recovery.—L. M. Chesney, *Lancet*, i/1926, 131.

Poisoning caused by about  $\frac{1}{2}$  oz. Cyanosis. Strychnine  $\frac{1}{10}$  gr. hypodermically and mustard 2 dr. by the mouth: after vomiting, stomach lavage.—P. Gibbin, *Brit. med. J.*, i/1927, 1005. See also *ibid.*, 1133, and A. Neale, *Brit. med. J.*, ii/1927, 520.

**Uses.** Antiseptic and deodorant. Oily spray solutions and ointments for use in catarrh are prepared with eucalyptus, pine oils and other ingredients such as menthol and camphor. It is also used for colds as a steam inhalation and given internally on sugar. Useful mixed with an equal quantity of olive oil as a rubefacient for rheumatism, and as an ointment for the treatment of burns.

**Nebula Eucalypti (B.P.C.).** Oil of eucalyptus 5% v/v in light liquid paraffin.

**Nebula Eucalypti Composita.**

Form A. Eucalyptus oil 5 m., cinnamon oil 2 m., menthol 12 gr., liquid paraffin containing 2% thymol iodide to 1 oz.

Form B. Eucalyptus oil 5 m., methyl salicylate 5 m., menthol 5 gr., liquid paraffin to 1 ounce for a common cold.

**Pigmentum Olei Eucalypti et Acidi Salicylici.**

Eucalyptus oil 8, salicylic acid 1, olive oil to 64.

Eczema capitis treated by rubbing into the scalp twice a week.

**Unguentum Eucalypti (B.P.C.).** 10% in a paraffin basis.

**Unguentum Eucalypti et Acidi Borici.**

Eucalyptus oil 40, boric acid 120, soft paraffin to 500. Lessens secretions of rhinitis.

**Unguentum pro Ustionibus.** *Syn.* TRINITY OINTMENT.

Eucalyptus oil 40 m., zinc ointment 120 gr., hydrous wool fat 120 gr., soft white paraffin to 1 oz.

**BURNS.** In second degree burns and scalds one expects to find the underlying skin soundly healed on removal of the (tannic acid) coagulum. Clean raw surfaces are treated with Trinity Ointment.—W. M. Dennison, *Lancet*, ii/1939, 1109.

**Vapor Eucalypti (T.H.).**

Oil of eucalyptus 20 m., light magnesium carbonate 10 gr., water to 1 ounce. A teaspoonful in a pint of hot water.

[P2] **Vapor Eucalypti Compositus (B.P.C.).** *Syn.* ANTICATARRHAL SALTS. Contains phenol, oil of eucalyptus, camphor, oil of Siberian fir, strong solution of iodine and ammoniated alcohol. Pine sawdust saturated with the mixture may be used as "smelling salts."

**Vap. Eucalypt. et Pini (N.I.F.).** Oil of eucalyptus 15 m., oil of Siberian fir 15 m., light magnesium carbonate 15 gr., camphor water to 1 oz.

**Eucalyptol (B.P., U.S.P. XI, P. Helv. V, Fr. Cx., F.E. VIII).** *Syn.* CINEOLE, CAJUPUTOL, MENTHAN-1:8-DIOL ANHYDRIDE.  $C_{10}H_{18}O = 154.1$ .

**Dose.**—1 to 3 minims (0.06 to 0.2 ml.). *U.S.P. XI* average dose 5 minims.

The principal constituent of oil of eucalyptus, which contains not less than 70%.

**Insoluble** in water; miscible with organic solvents and fixed oils.



It is preferred to the crude oil for use in oro-nasal inhalers owing to the fact that it is less irritating to the mucous membrane.

**Nebula Eucalyptolis Composita (B.P.C.).** *Syn.* NEBULA THYMOLIS COMPOSITA.

Eucalyptol 8% v/v, with camphor, menthol and thymol in light liquid paraffin.

**Pastilli Eucalyptolis (B.P.C.)** contain  $\frac{1}{4}$  m. (0.03 ml.).

**Pastilli Mentholis et Eucalyptolis (B.P.C.)** contain  $\frac{1}{2}$  gr. of menthol and  $\frac{1}{4}$  m. of eucalyptol.

**Eucalyptus (B.P.C.).** *Syn.* EUCALYPTI FOLIUM.

The dried leaves of *E. globulus* (Myrtaceae). Used in the form of the tincture in asthma, phthisis and chronic bronchitis.

**Tinctura Eucalypti (B.P.C.).** *Dose.*— $\frac{1}{2}$  to 2 drachms (1 to 8 ml.). 1 in 5. Haemorrhage from superficial wounds is stated to be capable of arrest by internal use of calcium chloride combined with local application of this tincture.

**Oleum Geranii (B.P.C.).** *Syn.* OIL OF ROSE GERANIUM, OIL OF PELARGONIUM. Obtained from the leaves of *Pelargonium odoratissimum*, *P. capitatum* and *P. Radula*. Used for perfuming dusting powders and other preparations.

**Oleum Graminis Citrati (B.P.C.).** *Syn.* INDIAN OIL OF VERBENA, OIL OF LEMON GRASS, INDIAN MELISSA OIL. Distilled oil from entire herb of *Cymbopogon citratus* and *C. flexuosus*. Carminative, with agreeable odour. Contains citral, citronellal, etc. True oil of verbena is from *Lippia citriodora* and has a more delicate odour.

**Herba Melissae (Fr. Cx., P. Dan.)** is from *Melissa officinalis* (Labiatae).

**Alcoolat de Mélisse Composé (Fr. Cx.)** is prepared from fresh flowering melissa, fresh lemon peel, cinnamon, clove, nutmeg, coriander and angelica root with alcohol 80%.

20 to 25 drops twice a day is also used as an application in rheumatism, etc.

**Oleum Juniperi (B.P.C.).** *Syn.* ESSENCE DE GENIÈVRE (Fr. Cx.).

*Dose.*— $\frac{1}{2}$  to 3 minims (0.03 to 0.2 ml.). Oil distilled from juniper fruits, *J. communis*. Sp. gr. 0.862 to 0.890, increasing with age. Soluble (when freshly distilled) 1 in 4 of alcohol 95%, becoming less soluble with age. A diuretic and urinary antiseptic, but should not be used in the presence of renal disease.

**Spiritus Juniperi (B.P.C.).** *Dose.*—5 to 20 minims (0.3 to 1.2 ml.). 1 in 10.

**Spiritus Juniperi Compositus.** *Dose.*—2 $\frac{1}{2}$  drachms. Oil of juniper 8, oil of caraway 1, oil of fennel 1, alcohol (99%) 1400, water to 2000.

**Vinum Diureticum (P. Helv. V.).** *Dose.*— $\frac{1}{2}$  to 1 ounce (8 to 30 ml.). Juniper 15, squill 10, orange peel 10, absinthe 5, angelica root 5, sweet flag 5, dry southern wine 1000.

**Juniperus (B.P.C., P. Dan.).** *Syn.* JUNIPER BERRY. The ripe fruits of *Juniperus communis* (Pinaceae) containing about 0.5 to 2% of volatile oil. Used principally in veterinary practice.

**Oleum Juniperi Lignl.** A trade name for fictitious juniper oil supposed to be made from the wood, but generally a mixture of juniper berry oil and oil of turpentine.

**Oleum Lavandulae (B.P., Fr. Cx.).**

*Dose.*—1 to 3 minims (0.06 to 0.2 ml.).

The oil distilled from the fresh flowering tops of *Lavandula officinalis* (Labiatae). English and French oils are available, the former being considered to have the finer odour. English oil

contains (*B.P. Add. I*) 7 to 12% *w/w* of esters, and French oil not less than 35% *w/w*, both calculated as linalyl acetate,  $C_{12}H_{20}O_2$ . English oil contains cineole which confers a distinctive odour.

Has carminative properties, and may be given internally (on sugar) in flatulence and colic. It is also used externally as an insect repellent.

**Spiritus Lavandulæ** (*B.P.C.*). *Dose.*—5 to 20 minims (0.3 to 1.2 ml.). 1 in 10.

**Spiritus Lavandulæ** (*U.S.P. XI*). *Average dose.*—30 minims (2 ml.). 1 in 20.

**Spiritus Lavandulæ Compositus** (*B.P.C.*). *Syn.* AQUA LAVANDULÆ. A form of lavender water for use in lotions, etc.

**Tinctura Lavandulæ Composita** (*B.P.C.*). *Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Oil of lavender 1 in 200, oil of rosemary, cinnamon, nutmeg and red sanders wood in alcohol 90%.

**Tinctura Lavandulæ Composita** (*U.S.P. XI*). *Average dose.*—30 minims (2 ml.).

Cinnamon 2, clove 0.5, nutmeg 1, red sanders 1, with oils of lavender and rosemary in diluted alcohol to 100.

**Oleum Lavandulæ Spicatæ** (*B.P.C.*). *Syn.* OIL OF SPIKE LAVENDER. From *L. latifolia* and other species. Has a harsher and more terebinthinate odour than oil of lavender, and is used for similar purposes.

**Oleum Melaleuca Alternifolia**. *Syn. and Prop. Names.* TI-TREE OIL, TEA-TREE OIL, AMBOL (*Australia Medical Products, Sydney*; *R. Ferber, London*), TI-TROL (*Australian Essential Oils Ltd., Sydney*; *Fassett & Johnson, London*).

The oil distilled from the Australian ti-tree, *M. alternifolia*, and containing about 50 to 60% of terpenes, including cineole (up to 8%) and terpineol, to which the odour is largely due. It is antiseptic and has been advocated as a non-irritant germicide for general and surgical use.

The Rideal-Walker coefficient is about 10.—A. R. Penfold, *Perfum. essent. Oil Rec.*, 1929, 155; also *Mfg. Chem.*, 1936, 332.

Although Penfold and Morrison have claimed that ti-tree oil has a R-W coefficient of 11 to 13, commercial brands available on the market have a coefficient of about 2 only.—W. C. Reynolds, *Chem. & Drugg.*, ii/1937, 615 and 697.

**Oleum Menthæ Piperitæ** (*B.P., Fr. Cx.*).

*Dose.*—1 to 3 minims (0.06 to 0.2 ml.).

Distilled from the fresh flowering tops of *Mentha piperita* (*Labiata*). Contains (*B.P. Add. I*) 4.0 to 9% *w/w* of esters calculated as menthyl acetate,  $C_{12}H_{22}O_2$  and not less than 46% of free menthol.

**Soluble** 1 in 4 of alcohol 70% and 2 in 1 of alcohol 90%; with some samples of oil the solution becomes turbid on addition of more alcohol 90%.

**Uses.** Internally it has a sedative effect on the stomach and a mild stimulating effect on the intestines. It relieves gastric and intestinal flatulence and colic and is employed with purgatives to prevent griping. It may be employed by inhalation in coryza in place of menthol. Applied externally it has a mild anæsthetic action, and has been employed in neuralgia.

Oil of peppermint, given by mouth to man, decreased the gastric secretion even if there was stimulation of the flow of gastric juice by an alcohol test meal or by histamine. The mode of action of the essential oil is obscure, but patients with peptic ulceration benefit from its administration.—J. Meyer and co-workers, *Arch. intern. Med.*, 1935, 56, 88.

**Aqua Menthae Piperitæ Concentrata (B.P.).** Dose.—5 to 15 minims (0.3 to 1 ml.).

Contains 2% v/v of oil and is approximately 40 times the strength of the distilled water.

**Aqua Menthae Piperitæ Destillata (B.P.).** Dose.— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.). Oil of peppermint 1, water 1500; distil 1000.

**Aqua. Mentha. Pip. (D.T.F.).** Triturate oil of peppermint 60 m., with talc 1 oz., and water sufficient to produce 160 oz.; filter.

**Emulsio Menthae Piperitæ (B.P.C.).** Dose.—5 to 20 minims (0.3 to 1.2 ml.). 1 in 10 of oil of peppermint emulsified in water with tincture of quillaia.

**Spiritus Menthae Piperitæ (B.P.).** Dose.—5 to 30 minims (0.3 to 2 ml.). 1 in 10 of alcohol 90%.

**Spiritus Menthae Piperitæ (U.S.P. XI).** Average dose.—15 minims (1 ml.). Oil of peppermint 10% in alcohol in which 1% of washed dried peppermint leaf has been macerated for 6 hours.

**Syrupus Menthae Piperitæ (B.P.C.).** Dose.— $\frac{1}{2}$  to 2 drachms (2 to 8 ml.). Concentrated peppermint water 1, syrup to 8.

**Mentha Piperita (B.P.C., U.S.P. XI, Fr. Cx.).** Syn. PEPPERMINT. Dose.— $\frac{1}{2}$  to 1 drachm (2 to 4 g.). The dried leaves and flowering tops of *Mentha piperita* (Labiatae).

**Oleum Menthae Viridis (B.P.C., U.S.P. XI).**

Dose.—1 to 3 minims (0.06 to 0.2 ml.).

Distilled from fresh flowering spearmint, *Mentha viridis*, and *M. crispata*. Contains 42 to 60% of carvone.

Forms a clear solution with an equal volume of 85% alcohol, the solution becoming turbid on further dilution.

**Aqua Menthae Viridis Concentrata (B.P.C.).** Dose.—5 to 15 minims (0.3 to 1 ml.). 2% v/v of oil. Is approximately 40 times the strength of the distilled water.

**Aqua Menthae Destillata (B.P.C.).** Dose.— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.). 1 in 1000.

**Spiritus Menthae Viridis (U.S.P. XI).** Average dose.—15 minims (1 ml.). Oil of spearmint 10%, in alcohol in which 1% of washed dried spearmint leaf has been macerated for 6 hours.

**Mentha Viridis (U.S.P. XI).** Syn. SPEARMINT, MINT. Dose.— $\frac{1}{2}$  to 1 drachm (2 to 4 g.). The dried leaves and flowering tops of *M. viridis*.

**Oleum Niaouli (Fr. Cx., P. Helv. V).** Syn. ESSENTIA EX NIAULI (F.E. VIII).

The oil obtained from the fresh leaves of *Melaleuca viridiflora* by distillation in steam. It contains 35 to 60% of cineole, and gives a clear solution with an equal volume of alcohol 80%, and with four times its volume of alcohol 70%.

**Oleum Niaouli Depuratum (Fr. Cx.).** Prop. Name. GOMÉROL (*Laboratoire du Gomenol, Paris; Coates & Cooper, London*). Prepared by heating Oleum Niaouli with sodium plumbate on a water-bath for three hours, and distilling.

It is given in rhinitis, laryngitis and other diseases of the respiratory tract, and is used in various forms as a general antiseptic. For injection purposes dilutions in olive oil are used, in strengths varying from 2 to 20%.

**Oleum Pulegii (B.P.C.).** *Syn.* OIL OF PENNYROYAL.

*Dose.*—1 to 3 minims (0.06 to 0.2 ml.), on sugar or in water.

Distilled from fresh pennyroyal herb, *Mentha Pulegium*. A yellow or greenish-yellow oil containing not less than 80% v/v of pulegone. Mildly irritant to the kidneys and bladder and reflexly excites uterine contractions; is used as an emmenagogue. Is reputed to produce abortion. **Oleum Hedeomæ** from *Hedeoma Pulegioides* has similar properties and is similar in composition.

**Antidotes.** Empty stomach by emetic or stomach tube. Give purgative dose of magnesium sulphate. Demulcent drinks freely. Keep patient warm; hot applications to abdomen. Stimulants, e.g., hot black coffee. Morphine,  $\frac{1}{2}$  gr. hypodermically, for pain. Saline infusion if necessary.

The inclusion of oil of pennyroyal in the Fourth Schedule to the Poisons Rules is recommended.—Report of the Inter-Departmental Committee on Abortion, H.M.S.O., 1939.

**Spiritus Pulegii (B.P.C.).** *Syn.* ESSENCE OF PENNYROYAL. *Dose.*—10 to 20 minims (0.6 to 1.2 ml.). 1 in 10.

**Mentha Pulegium.** *Syn.* PULEGIUM, PENNYROYAL. *Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 g.). The dried leaves and flowering tops of *M. Pulegium*.

**Oleum Rosæ (B.P.C., U.S.P. XI, P. Helv. V, Fr. Cx., P. Jap. V).** *Syn.* OTTO OR ATTAR OF ROSE. Distilled from the fresh flowers of *Rosa damascena*, cultivated in Bulgaria (3000 yield 1). A pale yellow, semi-solid crystalline mass.

**Rosettol.** An artificial otto, probably more penetrating than the natural oil. It is essentially free from stearoptene, i.e., is fluid at ordinary temperatures.

**Aqua Rosæ (B.P.C.).** Triple rose water diluted, immediately before use, with twice its volume of distilled water.

**Aqua Rosæ Triplex (B.P.C.).** The undiluted rose water of commerce.

**Aqua Rosæ Concentrata (B.P.C.).** Contains 1% of oil of rose, and is approximately 40 times the strength of rose water.

**Unguentum Aquæ Rosæ (B.P.C.).** Contains oil of rose, rose water, white beeswax, borax and almond oil.

**Unguentum Aquæ Rosæ (U.S.P. XI).** Spermaceti 12.5, white wax 12, almond oil 56, borax 0.5, rose water 5, water 14, otto of rose 0.02. It must be free from rancidity and is required to be stored in pure tin collapsible tubes.

**Unguentum Rosæ Album (B.P.C.).** *Syn.* CERATUM GALENI. Contains oil of rose, triple rose water, spermaceti, white beeswax and almond oil.

**Oleum Rosmarini (B.P., Fr. Cx., P. Jap. V).**

*Dose.*—1 to 3 minims (0.06 to 0.2 ml.).

Obtained by distillation from the flowering tops of *Rosmarinus officinalis*. Contains not less than 2% of esters calculated as bornyl acetate,  $C_{12}H_{20}O_2$ , and not less than 9% of free alcohols calculated as borneol,  $C_{10}H_{18}O$ . Is used, mainly in hair lotions, as **Spiritus Rosmarini**.

**Spiritus Rosmarini (B.P.C.).** *Dose.*—5 to 20 minims (0.3 to 1.2 ml.). 1 in 10. Occasionally used in hair lotions as a mild stimulant.

**Oleum Rūtæ (B.P.C.).**

*Dose.*—2 to 5 minims (0.12 to 0.3 ml.), in hot water or on sugar.

A pale yellow oil with unpleasant odour becoming pleasant in great dilution. Contains about 90% of methylnonylketone. An emmenagogue and antispasmodic. Has been given as an enema in mucilage of starch for paralytic ileus.

**Ruta** (*B.P.C.*, *P. Helv. V*). *Syn.* RUE (*Fr. Cx.*), HERBYGRASS. *Dose.*—10 to 30 grains (0.6 to 2 g.). The dried herb *Ruta graveolens* (*Rutaceæ*). The infusion has been used as an emmenagogue.

**Confectio Rutæ.** *Dose.*—1 to 2 drachms (4 to 8 g.). Fresh rue, caraway, bay berries, of each  $\frac{1}{2}$ , sagapenum  $\frac{1}{2}$ , black pepper  $\frac{1}{2}$ , honey 16. Add the first three in powder by degrees to the sagapenum melted in the honey with water q.s. Carminative and antispasmodic. Sometimes used as enema in infantile convulsions.

[P1-S1] **Oleum Sabinæ** (*B.P.C.*).

[P1] and [S1] "*Savin, oil of*"

*Dose.*—1 to 4 minims (0.06 to 0.24 ml.). A violent irritant; has emmenagogue and abortifacient properties. May cause hæmaturia and gastro-intestinal irritation.

The inclusion of oil of savin in the Fourth Schedule to the Poisons Rules is recommended. Oil of savin has no legitimate use of any importance.—Report of the Inter-Departmental Committee on Abortion, H.M.S.O., 1939.

[P1-S1] **Unguentum Sabinæ** (*B.P. '85*). Melt lard 16 and wax 3 on a water-bath, add bruised fresh savin tops 8, digest 20 minutes and express through calico. Freshly made has been used in conjunction with blisters in rheumatoid arthritis.

[P1-S1] **Sabina** (*B.P.C.*, *P. Helv. V*, *Fr. Cx.*). *Syn.* SAVIN, SABINÆ CACUMINA. *Dose.*—5 to 10 grains (0.3 to 0.6 g.). *P. Helv. V* and *Fr. Cx.* have max. single dose  $7\frac{1}{2}$  gr.; max. during 24 hours 15 gr. The fresh or dried young shoots of *Juniperus Sabina* (*Pinaceæ*). Properties are due to the oil.

The tops of *Juniperus sabina*, when taken orally in large doses, sometimes produce abortion, followed by fairly serious poisoning. Two fatal cases of such poisoning are discussed, in both of which death occurred without abortion having taken place. The oil of sabina is fixed in the lungs, liver, uterus and kidneys, especially in the lungs and kidneys.—M. J. Papavassiliou, per *J. Amer. pharm. Ass.*, 1935, A-342.

## OLEA EXPRESSA

Notes on fixed oils not included in the following sections are given under the drugs from which they are manufactured (*see Index*).

**Oleum Arachis** (*B.P.*, *P. Helv. V*, *P. Dan.*). *Syn.* OLEUM NUCIS, GROUND-NUT OIL, PEA-NUT OIL.

*Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.).

The oil expressed from the seeds of *Arachis hypogæa* (*syn.* GOOBER NUT, MANILLA GRAIN, CHINESE ALMOND). Slightly soluble in alcohol 90%, miscible with ether, chloroform and light petroleum. Resembles olive oil in properties and uses, and *B.P. Add. II* and *III* authorise its use, if desired, in place of olive oil, in a number of official preparations.

**Emulsio Olei Arachis** (*B.P.C.*). *Syn.* MARYLEBONE CREAM (IMPROVED). *Dose.*—1 to 2 drachms (4 to 8 ml.). A 50% emulsion of arachis oil containing 300 units of vitamin D per drachm.

**Emulsio Olei Arachis cum Glucoso** (*Gt. Orm. H.*).

Arachis oil 15 m., saccharated lime solution 4 m., acacia  $7\frac{1}{2}$  gr., oil of cassia  $\frac{1}{10}$  m., oil of clove  $\frac{1}{10}$  m., chloroform  $\frac{1}{10}$  m., liquid glucose 30 m., water to 1 dr.

**Oleum Gossypii Seminis** (*B.P.*).

*Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.).

The purified semi-drying oil expressed from the seeds of *Gossypium herbaceum* and other species of *Gossypium* (*Malvaceæ*).

It is a yellow, almost odourless liquid with a bland nutty taste. At temperatures below 12° solid fat separates, and if this has occurred the oil should be remelted and mixed before use. It is used for the same purposes as olive oil, especially externally, and *B.P. Add. II* authorises its use, if desired, in place of olive oil, in liniment of camphor, hydrous ointment, and compound ointment of mercury.

**Wesson Oil** is a high grade of cottonseed oil, largely used in America as salad oil, said to be superior to olive oil for making mayonnaise.

**Oleum Palmæ (B.P.C.).** A fat obtained from the fleshy portion of the ripe fruits of the palm tree, *Elæis guineensis*, being expressed after allowing the fruits to ferment. It is an orange to dark red fat with a somewhat violet-like odour. Is used in the manufacture of soap. It is also a valuable potential source of vitamin A, 1 lb. of palm oil containing roughly 0.6 of the vitamin A activity of a similar quantity of cod-liver oil.

**Oleum Rapæ (B.P.C., P. Dan.).** *Syn.* RAPE OIL, COLZA OIL. The refined oil expressed from the seeds of *Brassica campestris* and other species. A pale yellow, slightly viscous oil with unpleasant taste unless highly refined. Used occasionally in liniments in place of olive oil; largely used for burning and as a lubricant. Is used as an edible oil in India.

**Ravison Oil** is from a wild variety of *B. campestris* found near the Black Sea. It resembles rape oil but differs in chemical constants.

**Oleum Sesami (B.P., P. Helv. V).** *Syn.* BENNÉ OIL, GINGELLY OIL, TEEL OIL.

*Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.). Expressed from the seeds of *Sesame indicum* (Pedaliaceæ). A pale yellow oil not solidifying at 0°. Slightly soluble in alcohol 90%; miscible with ether, chloroform and light petroleum.

It does not readily turn rancid, is easily saponified even by cold process, is a semi-drying oil, neither gummy nor sticky, readily absorbed. It is thinner than cottonseed oil.

It may be used instead of olive oil in various parts of the Empire, and *B.P. Add. II* authorises its use, if desired, in place of olive oil in liniment of camphor, hydrous ointment and compound ointment of mercury.

**Oleum Sojæ (B.P.C.).** *Syn.* SOYA OIL, SOYA BEAN OIL, SOJA BEAN OIL, SOY OIL.

Obtained by expression from soya seeds, the yield being 10 to 12%. A yellowish or brownish oil, used for soap-making and for burning. It is also used as an edible oil.

**Soja (B.P.C.).** *Syn.* SOYA BEANS. The seeds of *Glycine Soja* (Leguminosæ), cultivated in China and Japan for human use and latterly in America and Europe, chiefly for forage. A method of use in the East is to boil until soft and then ferment in a warm cellar—the resulting “cheese” being known as “Natto.”

It contains 38.5% of protein (on dry) and 20% of fat. It contains practically no starch—said to be due to presence of a diastase. Has been used as an addition to diabetic dietary. Soy flour is even more serviceable, containing almost  $\frac{1}{2}$  more protein than the bean, this being due to the removal of the fibrous hulls, which contain but little protein. The seeds also contain the enzyme urease, which

converts urea into ammonium carbonate. It can be extracted by dilute alcohol or acetone and used in the determination of urea in blood or urine.

In 1898 only 8 varieties of soy beans were grown in U.S.A.; now there are 60 different varieties, the acreage having mounted from 500,000 in 1917 to 2,500,000 in 1934. The soy bean itself and soy bean flour are used in the preparation of a wide variety of foods for human consumption, including medicinal foods for infants, diabetic and obese individuals. Soy bean oil is used in many industrial products. Soy bean meal is used chiefly for animal feed and fertiliser. In 1934 Duke stated there were more than 250 different uses for soy beans (a list of 49 uses is given).—A. M. Olsen and L. E. Prickman, *Proc. Mayo Clin.*, 1936, 467.

**Soya Bean Milk.** The shells are removed after baking the beans overnight in 3 times their weight of water, then ground and boiled for 5 minutes and filtered through a sieve. To every 1000 g. of filtrate add 20 g. of starch previously made into a paste with some of the filtrate, 60 g. of sugar, 1.5 g. of calcium lactate, and 1 g. of salt. The addition of cod-liver oil is essential.—*Brit. med. J. Epit.*, i/1931, 93.

Beans of the mammoth yellow variety are cleansed, treated to remove unpleasant flavour and converted into a milky liquid. Malt syrup, lactose, cotton seed oil, mineral salts (Nemssalz), and calcium lactate are added and the mixture homogenised and spray-dried, being re-liquefied in the proportion of 35 gr. to 8 oz. of boiled water, providing a greyish-white "milk", in fine suspension, with about the same body as cows' milk. One ounce contains 28 Steenbock units of vitamin D. The "milk" was well tolerated and babies fed on it showed gain of weight and resistance to infection equal to that of milk-fed babies.—F. R. Rittinger and L. H. Dembo, per *Brit. med. J.*, i/1933, 378.

Owing to its relative cheapness the soya bean flour-milk mixture merits an extended trial in countries where for economic reasons a satisfactory substitute for breast milk has hitherto been unobtainable. It should be possible to market a milk-plus-flour powder at a price much lower than that of full-cream dried milk.—*Brit. med. J.*, i/1940, 982.

**Soyolk** (*Soya Flour Manufacturing Co., Rickmansworth*). A flour made from the soya containing 20% of fat, which does not turn rancid. It has 42% of protein, 25% of carbohydrates, principally sucrose and dextrin, no starch, and vitamins A, B, D, and E. Suggested as a basic food for infants, i.e., to blend with other ingredients and reduce the protein and increase the sugar, e.g., with lactose.

**Sobee.** A mixture of soya bean flour 67.5% and barley flour 9.5%, with olive oil 19%, sodium chloride 1.3%, and calcium 2.7%. Used as a milk substitute for infants with milk idiosyncrasy. Infants take it well, digest it, and thrive on it.—L. W. Hill and H. C. Stuart, *J. Amer. med. Ass.*, ii/1929, 986; See also *ibid.*, 989.

## OLEUM HYDNOCARPI

### B.P.

**Dose.**—5 to 15 minims (0.3 to 1 ml.) gradually increased to 1 drachm (4 ml.); by subcutaneous or intramuscular injection,  $\frac{1}{2}$  drachm (2 ml.) gradually increased to 75 minims (5 ml.).

Obtained by cold expression from the seeds of *Hydnocarpus Wightiana*, and occurs as a yellowish or brownish-yellow oil or soft cream-coloured fat. Contains glycerides of hydnocarpic and chaulmoogric acids. Oleum Hydnocarpi (*P. Helv. V*) is from *Hydnocarpus Kurzii* (see Oleum Chaulmoogræ). For further information regarding the sources and characters of various commercial *Hydnocarpus* and *Chaulmoogra* oils, see under Oleum Chaulmoogræ, p. 751, and in Vol. II.

**Soluble** almost completely in hot 90% alcohol, partly insoluble in cold; miscible in ether, chloroform and carbon disulphide.

**Uses.** Is given *per os*, or by subcutaneous or intramuscular injection in the treatment of leprosy. It is well tolerated if injections are made into healthy subcutaneous tissues, and rarely causes any reactions. Hydnocarpus oil is not suitable for intradermal infiltration over a large area. For this purpose the esters are preferable.

Hydnocarpus oil with 4% of creosote the cheapest and most effective remedy, and the one which did the maximum amount of good in all stages.—R. G. Cochrane, R.S.M. Discussion, *Brit. med. J.*, i/1927, 285.

Vaccines intravenously are useful in certain cases and in the third stage of the disease: hydnocarpus oil is the most efficient treatment in the first and second stages.—E. Muir, R.S.M. Discussion, *Brit. med. J.*, i/1927, 284; *Lancet*, i/1927, 339.

**Hydnocroel** (Smith, Stanistreet, Calcutta). Hydnocarpus oil with the addition of 4% of double distilled creosote.

**Sodii Hydnocarpas.** *Prop. Name.* ALEPOL (Burroughs Wellcome, London).

**Dose.**—1 ml. of a 3% solution (increased to 5 ml. or more) intramuscularly or subcutaneously; intravenously 1 ml. of 1% solution increased by 1 ml., up to 5 or 10 ml.

A mixture of the sodium salts obtained from the low-melting fraction of the acids of *H. Wightiana* oil.

Sodium hydnocarpate is specially convenient, but apt to cause endophlebitis and block the veins when given intravenously.—E. Muir, per *Brit. med. J.*, ii/1930, 1095.

Pain of subcutaneous injections markedly reduced by addition of glycerin—2.5 ml. of pure glycerin to 100 ml. of 3% sodium hydnocarpate solution containing 0.5% of phenol.—J. T. Jackson, per *Brit. med. J. Epit.*, ii/1932, 98.

A preparation worthy of more than passing attention is sodium hydnocarpate (Alepol) which, in many countries, is used as the drug for routine treatment.—E. Muir, *Int. J. Leprosy*, 1933, 441.

Intravenous injections up to 10 ml. of 5% solution the method of choice in "mass" treatment in the Yambio District of the Belgian Congo. Locally, trichloroacetic acid is used and ulcers dressed with hydnocarpus oil.—A. Cruickshank, *Leprosy Rev.*, 1932, 6.

Ionisation of the nasal mucous membrane, using Alepol, potassium iodide, and sodium chloride, in 1% solution, produces in many cases apparently complete cure of leprotic lesions in this site, an electrode being placed in each nostril and kept in position by bandages, and a current of 20 to 30 ma. passed for 20 to 30 minutes.—F. G. Rose, *Brit. med. J.*, i/1929, 148.

20 out of 152 cases of leprosy cured by Alepol and no symptoms of disease have recurred after lapses of 4, 5, or 6 years.—S. Lagoudaky, *J. trop. Med. (Hyg.)*, 1937, 77.

[P2-81] **Avenyl** (Burroughs Wellcome, London). 2-Myristoxy-mercuri-3-hydroxybenzaldehyde, a mercury preparation for the treatment of leprosy complicated by syphilis. Is soluble in hydnocarpus oil and in the ethyl esters of hydnocarpus oil, and may be administered as a 0.25% solution in hydnocarpus oil, or as a 0.5% solution in the ethyl esters in doses of 1 ml., increased to 4 ml. or more, in courses of 12 to 15 injections.

**Oleum Hydnocarpi Æthylicum (B.P.).** *Syn. and Prop. Name.* ETHYL ESTERS OF HYDNOCARPUS OIL, ETHYL HYDNO-CARPATE, HYDNESTRYLE (Smith, Stanistreet, Calcutta).

**Dose.**—5 to 15 minims (0.3 to 1 ml.), increasing gradually to 1 drachm (4 ml.). By subcutaneous or intramuscular injection,  $\frac{1}{2}$  drachm (2 ml.) gradually increased to 75 minims (5 ml.).

A colourless or faintly yellow oil with acrid taste. Prepared by saponifying the oil and precipitating the acids, dissolving them



in ethyl alcohol and esterifying by passing in hydrogen chloride.

Is used for the same purpose as hydnocarpus oil, either alone or mixed with an equal volume of olive oil with or without creosote 4%.

Intradermal injections of chaulmoogra and hydnocarpus esters should be accompanied by intramuscular to produce maximum effect. Big doses should be pushed where resistance is high—but doses above 10 ml. harmful.—R. Cochrane, *Trans. R. Soc. trop. Med. Hyg.*, 1931, 98.

The action of hydnocarpus oil and its preparations, injected intradermally, is largely due to the local irritation, which continues for some time, the esters remaining absorbed inside the local cells, causing breaking down and phagocytosis of the lepromatous material. There might also be some antigenic action.—E. Muir, *Trans. R. Soc. trop. Med. Hyg.*, 1931, 92.

No proprietary preparation of hydnocarpus oil or esters at present on the market is more effective than the pure oil and esters prepared in institutions. For this reason, and because of their greater cost, the preferential use of such preparations is not recommended. Hydnocarpus oil and its esters intramuscularly, subcutaneously and intradermally remain, so far as our present knowledge goes, the most efficacious drugs for the special treatment of leprosy (Report of the Sub-committee on Treatment to the International Congress of Leprosy, Cairo, March, 1938).—*Leprosy Rev.*, 1938, 150.

**Eulykol** (*Burroughs Wellcome, London*). Phenyl-ethyl esters of a selected fraction of the acids of hydnocarpus oil, or "phenylethyl hydnocarpate." *Dose*.—Commence with 0.1 ml. intradermally and a week later infiltrate the whole patch with 1 ml., repeating at weekly intervals until the nodules have disappeared. *Lupus vulgaris*.

**LUPUS VULGARIS**. Phenylethyl hydnocarpate of value by intradermal injection in the treatment of lupus vulgaris. Of 11 cases treated, clinical cure of affected patches was obtained in 7 and the other 4 showed satisfactory progress. The injections cause comparatively little pain and after treatment very little scarring is present.—N. Burgess, *Brit. med. J.*, ii/1935, 835.

Extremely encouraging results in 15 cases of lupus vulgaris.—J. E. Wallace, *Brit. med. J.*, i/1937, 1151.

**Oleum Chaulmoogræ** (*B.P.C., U.S.P. XI, Fr. Cx., P. Ned-V, P. Helv. V, P. Belg. IV, F.E. VIII*).

*Dose*.—5 to 15 minims (0.3 to 1 ml.), increased to 1 drachm (4 ml.) orally, in capsules, cod-liver oil, or milk; 30 minims (2 ml.), increased gradually to 75 minims (5 ml.) by subcutaneous or intramuscular injection. *F.E.* max. single dose 1 g.; max. in 24 hours 5 g. *U.S.P. XI* average dose 15 minims.

The oil (about 33%) expressed from the seeds of *Hydnocarpus Kurzii* (formerly *Taraktogenos Kurzii*). This is an evergreen shrub growing in Chittagong, Burma, and other parts. *U.S.P. XI* and *Fr. Cx.* include the oils of *Taraktogenos Kurzii*, *Hydnocarpus Wightiana*, *H. anthelmintica* and other species of *Hydnocarpus*, provided the oil agrees with specification. *P. Helv. V* calls this oil "Oleum Hydnocarpi," with *syn.* OLEUM CHAULMOOGRÆ.

The kalaw tree, frequently stated to be the historic origin of chaulmoogra oil, is apparently the Burmese name for *Taraktogenos Kurzii*.

Gynocardia oil is from *G. odorata*. It has a brown colour and odour resembling painter's varnish, and remains liquid down to 4.5°. It does not contain chaulmoogric acid but consists chiefly of the glyceryl esters of linolic and linolinic acids. It is stated to have no therapeutic value in leprosy. The fruits yielding genuine chaulmoogra oil are distinguished from those of gynocardia by

containing *many* seeds (average 21) packed closely together and faceted by mutual pressure, hence no two are the same identical shape, and having no pulp. The embryo of the seed is vertical and cordate, while that of gynocardia is lateral and reniform.

The name chaulmoogra has been sometimes misapplied to a smaller seed derived from *Hydnocarpus anthelmintica*, a native of Siam, where it is known as Lukrabao. This is exported to China and used there for leprosy in place of the true chaulmoogra, which may be regarded as the East Indian remedy. The oil is used by natives of Siam for cutaneous infections and contains 67·8% of hydnocarpic acid and 8·7% of chaulmoogric acid.

The oil from *Hydnocarpus Kurzii* is cold-drawn. It is a yellow fat, or at tropical temperatures a brownish-yellow oil with an odour of rancid butter and m.p. of 22° to 23°. It consists chiefly of the glycerides of chaulmoogric acid,  $C_{18}H_{32}O_2$ , and hydnocarpic acid,  $C_{16}H_{28}O_2$ . The residual cake is valuable for cattle feeding.

The oil from *Taraktogenos Kurzii* is often adulterated and other hydnocarpus oils are frequently sold as chaulmoogra oil. Because of these disadvantages its use in leprosy treatment has been largely superseded by *H. Wightiana* and *H. anthelmintica* oils which are cheaper and of better quality. Statements that the oil does not keep are untrue, but the oil is practically never expressed from fresh dried seeds, and oil from old seeds is always irritating.—H. I. Cole and H. T. Cardoso, *J. Amer. chem. Soc.*, 1939, 3442.

**Soluble** in ether and in chloroform.

**Uses.** Chaulmoogra oil is employed almost exclusively for the treatment of leprosy. It is not a specific, but with prolonged treatment (extending over several years) it results in so complete an arrest of the disease as to produce an apparent cure in a very considerable proportion of cases. It may be given by mouth (in capsules after meals), by intramuscular injection or by intradermal infiltration, or by a combination of these procedures. It has also been employed in pulmonary tuberculosis, but there is no convincing evidence of its clinical value, though successful results are claimed for its use by local application in tuberculous pharyngitis.

Externally, the oil is a potent rubefacient and may cause great pain when applied to raw surfaces, though a 30% ointment in lanolin has been used in chronic psoriasis.

INTRADERMAL INFILTRATION undoubtedly gives better results than intramuscular and subcutaneous injections in leprosy. In patients in whom the skin areas involved are too small to permit giving the desired doses by the intradermal route, supplementary intramuscular or subcutaneous injections may be given. The relative efficacy of the oil and esters given intradermally has not yet been fully tested, but experience shows that both are effective, and that if either is better than the other the difference is not great.

**Technique.** A small syringe is used with a short guarded needle. If oil is used the temperature must be at least 55°. The area to be injected is marked off with grease pencil and sterilised. Infiltration is made through multiple punctures 6 to 10 mm. apart, 0·5 to 1 mm. being injected at each puncture, so that to give the maximum 5 ml. dose some 80 to 100 punctures are required. The needle should be sloped at an acute angle with the skin surface and should not enter more than 2 or 3 mm. except for deeper lesions. In patients with marked fibrous nodules, begin treatment by infiltrating them (2 to 4 drops slowly injected into the middle of the nodule), treating the more diffuse lesions later. The dose varies according to tolerance, from 0·5 to 5 ml. once or twice a week.

Almost all skin areas showing either visible lesions or deep analgesia due to local invasion by *M. lepræ* are suitable for infiltration (this does not apply to analgesia of the extremities due to affection of the nerve trunks supplying them). When the lesions are widespread it is well to begin with the back of the trunk, as it is less sensitive. As a rule lesions should not be infiltrated a second time within a month. The induration caused by the previous infiltration must first be absorbed, lest much pain and even ulceration occur. Spots of hyperpigmentation remain at old sites of puncture and the new punctures should be made between them. Recommendation of the infiltration method does not exclude other supplementary methods of special treatment, e.g., hot baths, cauterisation, etc. In a patient who can tolerate maximum treatment and maintain a sedimentation index below 10, a good prognosis can generally be given.—E. Muir, *Int. J. Leprosy*, 1933, 442.

Treatment of leprosy—a valuable review with extensive bibliography.—E. Muir, *Int. J. Leprosy*, 1933, 407.

**TUBERCULOUS LARYNGITIS.** Local applications of chaulmoogra oil (Burmese), either diluted 10 to 20% in mineral oil, or full strength, dropped into the larynx or applied by a swab, in ulcerative tuberculous laryngitis, and superficial infiltrations, have been praised by R. M. Lukens, of Philadelphia. R. Scott Stevenson found it soothing but not of any curative benefit.—*Brit. med. J.*, ii/1933, 964.

Use of Indian chaulmoogra oil disappointing, but good results from Burmese oil (which contains a larger proportion of chaulmoogric acid). 65% of cases were improved and 25% greatly improved or cured.—R. Scott Stevenson, *Practitioner*, ii/1937, 565.

Chaulmoogra oil is the most effective local application, but the Burmese oil must be employed. Of 40 cases so treated, 2 were healed, 11 much improved, 15 improved, 6 remained stationary, and 6 became worse.—R. S. Stevenson and F. R. G. Heaf, *Brit. med. J.*, i/1940, 164.

#### **Emulsio Olei Chaulmoogræ.**

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Chaulmoogra oil 1 oz., poppy seed oil 2 oz., powdered acacia  $\frac{1}{2}$  oz., cinnamon oil 6 m., saccharin elixir 45 m., with water to make 6 oz.

#### **Injectio Olei Chaulmoogræ Intramuscularis.**

*Dose.*— $\frac{1}{2}$  to 1 ml., increased to tolerance.

Chaulmoogra oil and almond oil equal parts, sterilised.

This and other formulæ have been given intramuscularly, but the injection of oily preparations of chaulmoogra is often badly tolerated—causing abscess heart failure, etc.

The following is said to be *painless*. Chaulmoogra oil 90, olive oil 10, benzocaine 3. 5 ml. injected at body temperature in deltoid region, alternating semi-weekly with 8 ml. in buttocks.

#### **Unguentum Chaulmoogræ (B.P.C.).**

10% in a paraffin basis.

#### **Sodii Chaulmoogras (B.P.C.).** *Syn.* SODIUM GYNOCARDATE.

*Dose.*—1 to 3 grains (0.06 to 0.2 g.) in 3% solution by intramuscular or intravenous injection.

A mixture of the sodium salts of the fatty acids, or of a selected fraction of the fatty acids, of chaulmoogra oil. Occurs as a granular yellow or buff-coloured powder.

Good results in long-standing infection from the use of sodium chaulmoograte in sufficient quantity to saturate the system to the limit of toleration, treatment extending over months. Intravenously 0.04 g. given every second day, followed by an interval of 25 days after each 12 injections. In some cases a 1% or 1.5% solution was better tolerated than the 3% solution. Found to be one of the best anti-leprosy remedies, intense and rapid in action.—E. Balbi, *Brit. med. J. Epit.*, i/1927.

#### **Æthylis Chaulmoogras (U.S.P. XI).**

*Average dose.*—By mouth or by intramuscular injection, 15 minims (1 ml.).

A pale yellow oil prepared from chaulmoogra or hydnocarpus oil, or from the oil of *H. Anthelmintica* by the same method as *Oleum Hydnocarpi Æthylicum*, which it closely resembles.

When given by the mouth it is tolerated much better than the oil and for longer periods, since its taste and odour are not disagreeable and it does not give rise to gastric upset. The injections also are better tolerated than those of the oil and are less painful.

**Chaulmoogri et Hydnocarpi Æthylicum** (*Fr. Cx.*) resembles the *U.S.P.* preparation. It is insoluble in water, but soluble in alcohol and miscible with organic solvents.

**Iodised Ethyl Chaulmoograte containing 2% Iodine.**

*Dose.*—1 ml. intramuscularly has been reported on.—*See H. W. Wade and C. B. Lara, Lancet, i/1927, 599.*

**Antileprol** (*Bayer Products, London*). Ethyl esters of the fatty acid of chaulmoogra oil.

**Moogrol** (*Burroughs Wellcome, London*). A mixture of esters of the acids of the chaulmoogric series for intramuscular injection in the treatment of leprosy, and also, in combination with 4% of creosote, in lupus vulgaris. **Iodised Moogrol** is Moogrol with 0.5% of iodine, which markedly reduces the irritation produced. Injections are made intradermally and intramuscularly at weekly intervals. Intradermally, 5 ml. is given each time, 0.1 ml. at each point. If total 5 ml. cannot be given in this way, the balance is given intramuscularly.

## OLEUM MORRHUÆ

(with OLEUM HIPPOGLOSSI)

*B.P. Add. I, U.S.P. XI.*

*Syn.* OLEUM JECORIS ASELLI (*P.G. VI, P. Ital. V, P. Belg. IV, F.E. VIII, Fr. Cx., P. Dan.*), OLEUM JECORIS (*P. Helv. V*).

*Dose.*—Prophylactic, 15 to 30 minims (1 to 2 ml.) 3 times daily; therapeutic, 45 to 90 minims (3 to 6 ml.) 3 times daily. *U.S.P. XI* average daily dose 2 drachms (8 ml.).

The oil expressed from the fresh liver of the cod, *Gadus morrhua*, and freed from solid fat by filtration at 0°. *B.P. Add. I* and *Fr. Cx.* require the oil to contain per g. not less than 600 units of vitamin A activity, and not less than 85 units of antirachitic activity. These limits are much lower than the proportions of the two vitamins usually occurring in commercial samples of the oil (*see Vol. II*).

*U.S.P. XI* states "and other species of the family *Gadidae*." The oil may be flavoured with 1% of recognised flavouring agent. It contains at least 850 i.u. of vitamin A per g., and at least 85 i.u. of vitamin D.

**Soluble** slightly in alcohol 90%, miscible with ether, chloroform, and light petroleum.

**Uses.** Cod-liver oil is a valuable nutritive and is the most easily assimilated of all oils. It increases weight and improves the general condition of the patient. Its medicinal value is largely due to its high content of vitamins A and D. It is especially valuable in tuberculosis and other forms of wasting disease and is a specific in rickets. Externally the oil is sometimes applied by inunction with good results, especially to young infants. It is also applied externally in the treatment of burns, wounds, varicose ulcers, bed-sores, and inflammatory conditions of the eyes and

eyelids. Thus employed, the oil has a soothing action and stimulates epithelial growth. Ulcerative colitis has been successfully treated by rectal instillations of the oil.

**BURNS, VARICOSE ULCERS AND BED SORES.** 120 cases treated. A noticeable feature was the absence of pain when dressings were changed.—K. Strauss, *Dtsch. med. Wschr.*, 1935, 50.

Very popular with the patients, who experience great relief on its first application. A dressing of lint well soaked in crude cod-liver oil preferred to ointment. The dressing is soaked with the oil after 24 hours, the lint not being renewed until after 48 hours.—J. P. Steel, *Lancet*, ii/1935, 290.

Cod-liver oil, like other oily dressings, produces no coagulation of the damaged surface, and so allows the development of secondary shock and toxæmia.—W. M. Dennison, *Lancet*, ii/1939, 1107.

**BURNS OF THE EYELIDS.** The first dressing is a pad of lint saturated with the oil, covered with jaconet or oiled silk and a bandage, the patient being instructed to get a bottle of the oil and to keep the pad moist with it, leaving the pad undisturbed for 24 hours. There is never any septic discharge. The pad is changed every 24 hours. For use as drops at home, the easiest way is to pour the oil from a warmed teaspoon rather than use a dropper, which is difficult to keep clean, every 3 or 4 hours. One remarkable point is the almost instant relief from pain.—E. Stevenson, *Lancet*, ii/1935, 1376.

**EYE AFFECTIONS.** In addition to its use in burns of the lid and conjunctiva, cod-liver oil therapy is beneficial in corneal abrasions, dendritic ulcer, relapsing keratitis, degeneration due to mustard gas, blepharitis and general soreness of the lids.—E. Stevenson, per *Brit. med. J. Epit.*, ii/1936, 59.

For the treatment of the cornea, damaged by liquid mustard gas, the German Army use a mixture of cod-liver oil (emulsified with 1% sodium carbonate solution) and dextrose containing about 4% of pituitary (posterior lobe) extract.—J. H. Burn, *Brit. med. J.*, ii/1939, 972.

Dextrose and cod-liver oil ointment for the treatment of corneal ulceration caused by mustard gas may be prepared as follows: dissolve dextrose 3 dr., and sodium bicarbonate 30 gr., in water 2½ oz. Rub down anhydrous eucerin 240 gr., with cod-liver oil 1 oz., add 1 oz. of the aqueous solution and triturate briskly until emulsified. Gradually add the remainder of the aqueous solution and a further 2 oz. of oil with continuous trituration.—V. E. Benjafield, *Pharm. J.*, i/1940, 96.

The following is a satisfactory formula for cod-liver oil and dextrose cream. Cod-liver oil 3 fl. oz., eucerin anhydrous 5 dr., water 11 dr., dextrose 3 dr., sodium bicarbonate 30 gr. Melt the eucerin anhydrous at a temperature not exceeding 70°, add gradually a solution of the dextrose and sodium bicarbonate in the water, previously warmed to 60°, with constant trituration until emulsification is complete. The "primary" emulsion so formed is then diluted with the cod-liver oil to complete the preparation.—J. Morgan, *Pharm. J.*, i/1940, 112.

**GASTRIC ULCER.** Good results were obtained from the administration of cod-liver oil (20 g. 4 times daily) to patients with gastric ulcer when operative treatment was contraindicated. The best response was obtained when the ulcer was situated high in the lesser curvature and the ulcerative process had spread through to the neighbouring organs. Cod-liver oil leads to increase in weight, limits gastric motility and has a local therapeutic effect on the ulcerated tissue.—W. Löhr, per *Nutr. Abstr. Rev.*, Jan., 1936, 795.

**OSTEOMYELITIS.** Strikingly satisfactory results obtained in acute cases. The dressing is painless and need not be changed.—W. Löhr, *Dtsch. med. Wschr.*, 1936, 997.

**TUBERCULOUS PHARYNGITIS.** Tuberculous lesions of the throat and larynx respond well to spraying of the ulcerated areas three times a day with cod-liver oil. Of 91 patients so treated 27.5% were healed, 46.2% were improved subjectively and objectively, and 26.3% remained unimproved.—A. L. Banyai, per *Brit. med. J. Epit.*, i/1938, 97.

**ULCERATIVE COLITIS.** Ulcerative colitis successfully treated by retention enemata of cod-liver oil, using an initial dose of 2 oz. and increased by 2 oz. at a time to a maximum of 8 oz.—H. Gainsborough, *Lancet*, i/1939, 1319.

Rectal instillation of a 40% gum emulsion or 68% suppositories used for ulcerative colitis. Improvement noted in 9 out of 11 patients.—R. Spiegel, *Journal of Mt. Sinai Hospital, New York*, per *Amer. J. Pharm.*, 1938, 132.

**WOUND TREATMENT.** Three years' experience of the application of fresh unheated cod-liver oil, mixed with an indifferent oily medium to the consistency of a paste, to suitable wounds, e.g., recent uninfected accidental wounds, burns, compound fractures, amputation wounds, bed-sores, frostbite, etc. Dressing changed as infrequently as possible, and contact of the wound with the inner portion of the dressing left undisturbed.—W. Löhr, per *Brit. med. J. Epit.*, ii/1934, 86.

Treatment of 300 casualty cases from an explosion at a toluol factory, including badly infected compound fracture, open wounds of the joints, extensive muscle and tendon lacerations, complete removal of the scalp, and severe burns. The immediate surroundings of a wound having been shaved clean, it was filled with a cod-liver oil ointment and then lightly secured with sutures made from the muscles of horses and cattle. Over this was a layer of cod-liver oil ointment, kept in place by an adhesive dressing. Necrotic tissues quickly came away and the depths of the wound became filled with granulation tissue. The ease with which new skin grew rendered transplantation superfluous, although there had been no preliminary sterilisation.—P. Bosse, *Dtsch. med. Wschr.*, 1935, 1638.

In the treatment of injuries affecting a very large area, special reference being made to the requirements of war surgery, the method which consists in excising the wound, filling it with pure vitamin A oil or ointment, and immediately applying a plaster of Paris dressing, constitutes a real advance.—S. Sandor, *Lancet*, ii/1936, 740.

Subcutaneous injection of fish liver oils into rabbits produces a marked stimulation of phagocytes, fibroblasts, and young capillaries. Liquid paraffin and olive oil are relatively inert. The vitamin A content of the oils is not responsible for this reaction. The cellular stimulation produced by cod-liver oil appears to facilitate the process of healing wounds.—J. Davson, *Lancet*, ii/1936, 738.

It is established that cod-liver oil has definite bactericidal power, and irradiation with ultra-violet rays greatly enhances this power. It is further established that the bactericidal action of an oil is closely related to its content of peroxides which is also increased by irradiation. The merits of cod-liver oil dressings are emphasised and a clinical trial of irradiated oil advocated.—M. Lichtenstein, *Lancet*, ii/1939, 1023.

**Controlled Cod-liver Oil Mixture** (*B.S.S.* No. 910—1940) is a preparation of cod-liver oil for animal feeding. It is produced only under licence granted by the Ministry of Food under the Cod-liver Oil (Control of Production) Order, 1940, and consists of veterinary cod-liver oil of a high vitamin potency diluted with a suitable marine oil, preferably of animal origin, supplied by the Ministry of Food. Controlled cod-liver oil mixture should contain not less than 600 i.u. of vitamin A and 85 i.u. of vitamin D per g.

**Oleum Morrhuæ Aromaticum.**

*Dose.*—1 to 4 drachms.

Coumarin 0.01, saccharin 0.5, vanillin 0.6, dehydrated alcohol 10.0, oil of lemon 20.0, oil of peppermint 3.0, cod-liver oil to 1000. The taste is covered but the odour persists to some extent.

**Oleum Jecoris cum Iodo.** *Syn.* OLIO DI FEGATO DI MERLUZZO IODATO (*P. Ital. V*). Contains 0.05% of iodine dissolved by trituration. *P. Helv. V* has 0.01%.

**Oleum Morrhuæ Non-Destearinatum** (*U.S.P. XI*) is the entire oil, i.e., not destearinated.

**Emulsio Olei Morrhuæ** (*B.P. Add. II*).

*Dose.*—Prophylactic,  $\frac{1}{2}$  to 1 drachm (2 to 4 ml.), approximately equivalent to 1000 to 2000 units of vitamin A and 100 to 200 units of vitamin D. Therapeutic,  $1\frac{1}{2}$  to 3 drachms (6 to 12 ml.), approximately equivalent to 3000 to 6000 units of vitamin A and 300 to 600 units of vitamin D.

Contains 50% v/v of cod-liver oil. *B.P.C.* is similar but has *dose*— $\frac{1}{2}$  to 1 ounce (8 to 30 ml.).

Loss of vitamin A depends more on conditions and time of storage than on method of preparation. The emulsion must be protected against light, heat and air, and is preferably stored in well-filled brown bottles at a temperature below 15°. There is no objection to the use of corks.—H. Lindholm, *Arch. Pharm. Chem.*, 1940, 47, 1.

**Emulsum Olei Morrhue (U.S.P. XI).**

*Average daily dose.*—Infants and adults, 4 drachms (15 ml.). If the content of vitamins A and D exceeds the U.S.P. minimum, the dose may be lowered proportionately.

Cod-liver oil 50%, with acacia and syrup and 0.4% of methyl salicylate, or not more than 1% of any other flavouring agent prepared with recognised substances. Agar, gelatin, tragacanth or mixture of these may be used instead of acacia, and if the emulsion is stored 7% of water should be replaced by alcohol.

**Emulsio Olei Morrhue et Creosoti (B.P.C.).**

*Dose.*— $\frac{1}{2}$  to 1 ounce (8 to 30 ml.). Contains 33 $\frac{1}{3}$ % v/v of cod-liver oil with 4 m. of creosote per oz.

**Emulsio Olei Jecoris Ferrata (P. Svec. X)** has cod-liver oil 300, calcium hypophosphite 6, citric acid 2, iron pyrophosphate with ammonium citrate 9, acacia 53, syrup 60, vanillin 0.6, dissolved in dilute alcohol 5 and water to 600.

**Ferrated Emulsion of Cod-Liver Oil** consists of the plain emulsion with iron and ammonium citrate 5 gr. per oz.

**Emulsion of Cod-Liver Oil with Glycerophosphates**, v. p. 46.

**Emulsio Olei Morrhue cum Hypophosphitibus (B.P.C.).**

*Syn.* EMULSIO OLEI MORRHUE COMPOSITA.

*Dose.*— $\frac{1}{2}$  to 1 ounce (8 to 30 ml.).

Cod-liver oil 50% v/v with 1 gr. each of sodium and calcium hypophosphites per dr.

**Emulsio Olei Morrhue cum Ovocithino** is the above with 5 gr. of lecithin per oz. *Dose.*—2 to 8 drachms (7 to 30 ml.).

**Unguentum Zinci Morrhuatit (B.P.C.).** Contains about 14% of cod-liver oil, with zinc oxide, talc, and balsam of Peru in a basis of wool fat, solution of calcium hydroxide, beeswax and soft paraffin.

Cod-liver oil ointments may be prepared from the following formulæ, the waxes and other ingredients being melted first and the cod-liver oil added gradually at temperatures of 30° to 35°, avoiding the formation of air-bubbles. (a) White beeswax 10 g., spermaceti 10 g., cod-liver oil 80 g. (b) Yellow beeswax 20 g., soft paraffin 50 g., cod-liver oil 40 g.; this is very suitable for wounds and sores. (c) Beeswax 20 g., stearic acid 20 g., soft paraffin 30 g., hydrous wool fat 30 g., cod-liver oil 100 g. (d) Yellow beeswax 10 g., triethanolamine stearate 10 g., hydrous wool fat 25 g., cod-liver oil 75 g.; talc or zinc oxide can be added to this to increase its curative and cicatrising actions.—A. Ferraris, per *Quart. J. Pharm.*, 1939, 642.

**Coco-Vitamin (Lilly, London).** Cod-liver oil 40%, vitamin B extract 40%, malt extract 10%, potassium hypophosphite 1.7% with chocolate and aromatics. 1 oz. contains vitamin A 5500 units, B 16 units, D 1300 units.

**Cytobiase (Bengué, London).** Drops containing cod-liver oil extract 40 g. and excipient to 100 g. 25 drops = 4 oz. of cod-liver oil. *Dose.*—For adults 25 to 30 m. twice daily before meals.

**Cod-Halibut-Liver Oil, 10 D (Allen & Hanburys, London).** Cod-liver oil mixed with halibut-liver oil and containing vitamin A 10,000 units per g., vitamin D 1000 units per g.

**Desitin (Coates & Cooper, London).** Preparation of cod-liver oil for external use. Supplied as ointment or dusting powder for the treatment of burns, eczema, wounds, etc.

**Jecocin (Boots, Nottingham).** Medicated cod-liver oil, containing creosote, chloroform, cinnamon oil and amylmeta-cresol. *Dose.*—1 teaspoonful 3 or 4 times daily: not suitable for children. Infections of the lung and bronchi, e.g., chronic bronchitis, bronchiectasis, emphysema, etc.

**Morelix (Gale, Bais, London).** A combination of cod-liver oil with malt, hypophosphites, Virginian prune, and aromatics. A nutritive tonic.

**Morvette Cod-liver Oil Tablets** (*A. H. Cox, Brighton*) contain vitamin A, cholesterol and lipochrome-containing bodies, also phosphorus, bromine and iodine.

**Reinforced Cod Liver Oil** (*Pharmaceutical Specialities (May & Baker) Ltd., London*). Contains per ml. 2000 i.u. of vitamin A and 500 i.u. of vitamin D.

**"SevenSeas" High Potency Oil** (*British Cod Liver Oil Producers, Hull*). Natural cod-liver oil four times as rich in vitamins as cod-liver oil, *B.P.* Dose.—5 minims. Also supplied in 5 m. capsules.

### **Sodii Morrhuas** (*B.P.C.*).

**Dose.**—*Subcutaneously*  $\frac{1}{2}$  ml. of a 3% solution slightly increased up to 2 ml., 2 or 3 times a week until reaction (febrile and local) occurs. When 2 ml. has been reached give this dose *intramuscularly* up to 4 ml.

For *intravenous* use as a sclerosing agent, *v. postea*.

Sodium morrhuate consists of a mixture of the sodium salts of the fatty acids or of a fraction of the fatty acids of cod-liver oil, prepared by the hydrolysis of cod-liver oil with sodium hydroxide. It is purified by extracting with ether. Sodium morrhuate is a light brown powder with a slightly fishy taste.

**Soluble** in warm water; almost completely soluble in alcohol (90%). The 10% aqueous solution should be clear.

**Storage.** It should be kept in well-closed containers, preferably stoppered bottles, and the making and stocking of large quantities is inadvisable. It is considered that the insolubility and darkening in colour of old samples of sodium morrhuate is due to hydrolysis rather than to oxidation, although the latter may also occur.—G. W. G. Smithers, *Quart. J. Pharm.*, 1938, 537.

**Uses.** Sodium morrhuate was originally used in the treatment of leprosy. It has also been administered as a 3% solution by injection in the treatment of lupus and tuberculosis. In none of these conditions, however, have the original claims as to its value been substantiated and it is now used chiefly as a sclerosing agent in the injection treatment of varicose veins. In most cases a 5% solution of sodium morrhuate is strong enough to obliterate the lumen with a minimum amount of inflammation. It causes strictly localised mild inflammation of the vein wall, followed by firm fibrous occlusion of the vessel. The size of the vein is the determining factor as to the dosage. In small or medium-sized veins 1 or 2 ml. is sufficient, while in large veins 3 to 5 ml. is necessary. The total dose should not exceed 10 ml. The injection of 2 to 5 ml. of the 5% solution, following aspiration, is also stated to give good results in the treatment of hydrocele.

Solid matter may separate from the solutions on standing, but redissolves on warming. The syringe should be warmed before filling with the solution.

**Technique of Injection in Varicose Veins.** Sodium morrhuate appears to be most effective when injected into a not fully distended vein; the patient is therefore best treated in a horizontal position by elevating the limb, and then applying digital pressure or a tourniquet above the point of injection. The standing position may be of advantage in the treatment of smaller veins. The effect on the injected vein is usually prompt. A few minutes after the injection



the vein begins to harden below the site of injection for about 2 to 4 inches. Injections are given at 24 to 48-hour intervals, according to the response of the patient to the drug.

GANGLIA treated by sodium morrhuate injections 5%, 0.2 to 5 ml., after aspiration.—Peter McEvedy, *Lancet*, ii/1930, 902.

HÆMORRHOIDS injected with sodium morrhuate.—A. S. Ross, *Brit. med. J.*, ii/1930, 86.

Two cases of severe anaphylaxis attending the use of sodium morrhuate for injection of hæmorrhoids.—N. J. Simmons, *New Engl. J. Med.*, i/1938, 527.

HYDROCELES, providing they are primary and have not been caused by some lesion of the testicle, react well to aspiration and subsequent injection of 2 ml. of a 5% solution of sodium morrhuate.—David Levi, *Practitioner*, i/1936, 506.

Drain off all the fluid after first anæsthetising with 2% Novocaine. Wash out the sac with 5 to 10 ml. of distilled water to remove albuminous fluid adhering to the walls of the sac. Examine the testicle—only if it is normal in size and shape is injection indicated. Then inject from 2 to 5 ml. of 5% sodium morrhuate; the amount required varies with the size and duration of the hydrocele and the consistency of its walls. After injection the scrotum should be actively massaged for 2 or 3 minutes so that the fluid is distributed as a coating over the walls of the sac. The puncture is sealed with collodion gauze and a scrotal support fitted. In carefully chosen cases one can safely predict 80% of cures. The likely failures are the very long-standing thick-walled sacs.—A. E. Porritt, *Med. Pr.*, ii/1936, 27.

VARICOSE VEINS. The most popular injection for varicose veins at St. Mary's Hospital is a 5% solution of sodium morrhuate in 0.5% phenol; 13,000 ml. of this solution was made during 1935.—C. M. Wilson, *Practitioner*, i/1936, 653.

Sodium morrhuate is definitely dangerous for intravenous injection. A case of sudden death in an elderly woman has been reported following injection of 2 ml., and other fatalities are reported in the literature.—David Levi, *Practitioner*, i/1936, 506.

Sodium morrhuate for veins not entirely free from danger.—A. H. Winchester, *Brit. med. J.*, ii/1930, 120. Urticariiform wheals with pain for a week.—T. H. Treves-Barber, *ibid.*, 60, 195.

Sodium morrhuate thought to lead at times to immediate thrombus formation.—Reginald Payne, *Brit. med. J.*, i/1932, 237.

Sodium morrhuate must owe its very wide popularity as a sclerosing agent to the frequency with which 0.5 ml. may be spilled in perivenous tissues without subsequent trouble. Of the three agents, morrhuate, quinine, and salicylates, morrhuate is by far the least locally harmful, and experimental evidence suggests it is the most efficient. Its chief disadvantage is the occurrence in certain patients of morrhuate sensitivity. There may be immediate and profound collapse; more often this sensitivity is shown by a diffuse eczematoid skin reaction which itches intensely and lasts 2 or 4 weeks. Morrhuate sensitivity may be found in about 5% of cases.—P. Clarkson, *Lancet*, ii/1938, 69.

Three cases of severe allergic reaction, one of which came near to a fatal outcome.—G. A. Holland, *Canad. med. Ass. J.*, ii/1939, 262.

### **Injectio Sodii Morrhuatii (B.P.C.).**

*Dose*.—8 to 75 minims (0.5 to 5 ml.) intravenously.

Sodium morrhuate 5, alcohol 90%, 1, water to 100.

Solutions for injection should only be made from sodium morrhuate that answers the B.P.C. test for solubility. The addition of benzyl alcohol is more effective than the addition of ethyl alcohol, and if solutions are buffered at pH 9.6 they clear readily on gently warming. The following formula is suggested: sodium morrhuate 5 g., benzyl alcohol 2 ml., boric acid 0.31 g., sodium hydroxide 0.085 g., water to 100 ml. Dissolve the sodium morrhuate with gentle warming in a solution of the boric acid and sodium hydroxide in about 80 ml. of water. Cool, add the benzyl alcohol, shaking well until dissolved, adjust to volume and filter. It may be sterilised by autoclaving at 120° for thirty minutes.—G. W. G. Smithers, *Quart. J. Pharm.*, 1938, 536.

**Varicane** (*Pharmaceutical Specialities (May & Baker) Ltd., London*).  
Solution of sodium morrhuate 5% and 10% for varicose vein injection.

See also quinine and urethane, sodium chloride, and sodium salicylate for other sclerosing agents for varicose veins.

**Oleum Hippoglossi** (*B.P. Add. II*).

*Dose*.—1 to 5 minims (0.06 to 0.3 ml.), approximately equivalent to 1500 to 7500 units of vitamin A.

The fixed oil extracted from the fresh or suitably preserved liver of the halibut *Hippoglossus vulgaris*. A pale to golden yellow liquid with a fishy odour and taste.

**Soluble** slightly in alcohol 90%, and miscible with ether, chloroform and light petroleum.

The oil is particularly rich in vitamin A, but the vitamin content of the natural oil varies widely (*for details see Vol. II*). *B.P. Add. II* requires a content of not less than 30,000 units of vitamin A activity per gramme. For commercial purposes the oil is adjusted by admixture with weaker oil or with a vegetable oil, and vitamin D is added so that the content of this vitamin, which varies between 2500 and 3000 units per g. bears a definite relationship to that of good cod-liver oil.

**Halibol** (*Allen & Hanburys, London*). Halibut-liver oil with added vitamin D. Vitamin A 60,000 i.u. and vitamin D 10,000 i.u. per g. *Dose*.—2 to 4 drops twice or thrice daily after food. Also supplied in 3 m. capsules either plain, or as **Halibol-B**, containing the addition of vitamins B<sub>1</sub> and B<sub>2</sub>, equivalent to 5 gr. of yeast, or as **Halibol-Calcium**, containing the addition of calcium-sodium lactate 5 gr. **Halibol Malt** is extract of malt with halibut-liver oil, containing twice the proportions of vitamins A and D present in extract of malt with cod-liver oil *B.P.*

**Haliborange** (*Allen & Hanburys, London*) is a mixture of Halibol and concentrated orange juice. *Dose*.—1 to 8 drachms daily, according to age.

**Haliver Oil Plain** (*Abbott Laboratories, London*). Halibut-liver oil containing vitamin A 50,000 i.u., and vitamin D 850 i.u. per g. **Haliver Oil with Viosterol** is halibut-liver oil with viosterol, and contains vitamin A 50,000 i.u., and vitamin D 10,000 i.u. per g. **Haliver Malt with Viosterol** contains Haliver oil, viosterol, calcium, phosphorus, liver extract and malt.

**Halidexol** (*Crookes Laboratories, London*). Halibut-liver oil emulsion. Each teaspoonful contains 6200 i.u. vitamin A, 220 i.u. vitamin D.

**Halimalt** (*Crookes Laboratories, London*). Halibut-liver oil in malt extract. Each teaspoonful contains 4300 i.u. vitamin A, and 420 i.u. vitamin D.

**Haliverol** (*Parke, Davis, London*). Halibut-liver oil with added vitamin D. The vitamin D potency is stated to be 250 times and the vitamin A potency 60 times, that of cod-liver oil. *Dose*.—3 to 5 minims three times a day. Children 5 to 10 minims daily. Also available in capsules.

**Halivitan** (*Richter, London*). Halibut-liver oil preparations. Liquid contains 40,000 i.u. of vitamin A per ml. *Dose*.—5 to 10 m. thrice daily. Tablets contain 4000 i.u. of vitamin A in each. *Dose*.—1 or 2 tablets thrice daily.

**Halivite** (*Scott & Bowne, London*). Halibut-liver oil in pills and liquid.

**Halycalcyne** (*Crookes Laboratories, London*). Halibut-liver oil with calcium phosphate. A useful adjunct in treatment of chilblains and for dental caries.

**Halycitrol** (*Crookes Laboratories, London*). Halibut-liver oil, orange juice and glucose.

**Nadola** (*Parke, Davis, London*). Standardised preparations of vitamins A and D from halibut-liver and other fish-liver oils. Available as liquid, containing 55,000 i.u. of vitamin A and 5500 i.u. of vitamin D per g., and as capsules, each containing 9400 i.u. of vitamin A and 940 i.u. of vitamin D. *Dose*.—1 capsule (6 minims), or more, daily.

**Oleum Percormorphum** (*Mead, Johnson, Evansville, U.S.A.; Brooks & Warburton, London*). A mixture of the liver oils of various species of *percomorphi*, which is 100 times richer than cod-liver oil in vitamins A and D. Supplied in capsules and liquid.

**Super-D Oil** (*Crookes Laboratories, London*). Natural fish oils from fish of the order Scombridae, containing approximately 50,000 i.u. per g. of both vitamins A and D.

**Vitapan** (*Paines & Byrne, London*). Halibut-liver oil standardised to contain 35,000 i.u. of vitamin A and 7,500 i.u. of vitamin D per gramme. Supplied in perles and liquid. **Vitapan Co. Tablets** contain Vitapan  $\frac{1}{2}$  m., parathyroid  $\frac{1}{10}$  gr., and calcium glycerophosphate. **Vitapex Liquid** contains 35,000 i.u. of vitamin A and no vitamin D. Also supplied in capsules.

**Mutton Bird Oil**, the oil of the young sooty petrel, collected on the Stewart Island, south of New Zealand, has been advocated as a substitute for cod-liver oil in phthisis and bronchitis.

With a rachitogenic diet 2% of cod-liver oil could be replaced by 1% mutton bird oil. The latter was superior in growth-promoting value but for bone calcification the cod-liver oil appeared to be more satisfactory. Mutton bird oil at the rate of  $\frac{1}{4}$ % failed to prevent rickets.—per *Nutr. Abstr. Rev.*, Apl., 1936, 1151.

Various specimens of the oil estimated by colorimetric methods show the vitamin A content to be of a very low order, and it is therefore virtually useless as a medicinal source of vitamin A. Its vitamin D content is also very low.—per *J. Amer. med. Ass.*, ii/1939, 871.

**PULMONARY TUBERCULOSIS.** A 33% emulsion recommended. Administration of the oil is stated to give very gratifying results. Description of the mutton bird (*Puffinus sp.*).—J. H. Blackburn, *Brit. med. J.*, ii/1936, 949.

An emulsion of mutton bird oil has been found to give good clinical results in pulmonary tuberculosis, there being increased weight, loss of cough, diminished sputum, and a general improvement. 100 patients treated.—J. H. Blackburn, *Brit. J. Tub.*, 1937, 285, per *Practitioner*, i/1938, 329.

**Whale Oil.** The oil obtained by boiling with water, the blubber of various species of *Balaena*. The best quality, known as Whale Oil No. 0, is of a pale yellow colour with a faintly fishy odour. The term "train oil," formerly applied to whale oil is now extended to the oil from the blubber of any marine animal, including seals.

**Uses.** Whale oil is used as a solvent for vitamins in medicinal preparations, for soap-making and as a burning oil. Hydrogenated whale oil is used in margarine manufacture.

## OLEUM OLIVÆ

*B.P., U.S.P. XI, P. Helv. V, Fr. Cx., etc.*

**Dose.**— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.).

The oil expressed from the ripe fruit of *Olea europæa* (Oleaceæ).

Inferior brands are obtained by addition of the pulped fruit to boiling water and by fermentation processes. The *B.P.* requires an acid value of not more than 2.0, but permits the use of an oil having an acid value of not more than 6.0 in making official liniments, ointments and plasters.

**Uses.** Internally, olive oil is nutrient, demulcent and mildly laxative. It retards the flow of the gastric juice and is an excellent food in gastric and duodenal ulcer, being given either by the mouth or by stomach tube. It often gives relief to patients suffering from cholecystitis, from 2 to 8 fl. oz. being taken in divided doses during the day. As a laxative, from 4 to 8 fl. oz. are taken daily. It may also be given by rectal injection (5 to 20 fl. oz. warmed to about 90°F) in chronic constipation and to remove impacted faeces. Chronic colitis has been treated by retention enemas of 8 to 10 fl. oz. of the warm oil, continued nightly for a fortnight.

Externally, olive oil is emollient and soothing to inflamed surfaces, and is employed to soften the skin and crusts in eczema and psoriasis, and as a lubricant for massage. It has also been

employed as a protective to burns, but its use in this manner is condemned, since it facilitates bacterial growth.

In preparing emulsions of olive oil of low acid value for external use, *e.g.*, with lime water, a few drops of oleic acid may be necessary in order to produce sufficient calcium oleate to act as emulsifying agent.

A tablespoonful flavoured with peppermint before meals of value in digestive disorders and heartburn.—W. Morrell Roberts, per *Lancet*, i/1931, 537.

**Emulsio Olei Olivæ (B.P.C.).**

*Dose.*— $\frac{1}{4}$  to 1 ounce (8 to 30 ml.). Contains 50% of olive oil.

**Enema Olei Olivæ (B.P.C.).** *Dose.*—20 ounces (600 ml.). 20% v/v in mucilage of starch. Undiluted, 5 to 20 ounces (150 to 600 ml.).

**Enema Oleosum (L.H.).** Olive oil 4, soft soap 1, warm water 16.

**Huile d'Olive Neutralisée et Sterilisée (Fr. Cx.).** Olive oil warmed with a sufficient quantity of sodium carbonate to neutralise it, and filtered. It is used in the preparation of oil solutions for injection, and before use must be heated to 135° to 140°.

**Unguentum Aquosum (B.P.).**

Distilled water 24, borax 1, olive oil 50, with white beeswax and white soft paraffin.

*B.P. Add. II* allows the use of either arachis, cottonseed or sesame oil instead of olive oil in making hydrous ointment.

**Oleum Maydis (U.S.P. XI). Syn. CORN OIL.**

The refined oil expressed from the germ of *Zea Mays* (Gramineæ). A light yellow oil slightly soluble in alcohol, miscible in all proportions with ether, chloroform, benzene and light petroleum. Sp. gr. 0.914 to 0.921. In Australia it may be used as a substitute for olive oil in *B.P.* and *B.P.C.* formulæ.

**Oleum Papaveris (Fr. Cx.). Syn. POPPY-SEED OIL, MAW OIL.**

The refined oil obtained by cold expression from the seeds of *Papaver somniferum*. A light yellow liquid, odourless and possessing a faint almond flavour. It is a drying oil, and is **soluble** in chloroform, ether and light petroleum.

*Uses.* Poppy-seed oil is used in *Oleum Iodisatum*, and as a substitute for olive oil.

## OLEUM RICINI

*B.P., U.S.P. XI, P. Helv. V, Fr. Cx., etc.*

*Dose.*—1 to 4 drachms (4 to 16 ml.). Doses of 1 fl. ounce (30 ml.) are often administered. *U.S.P. XI* average dose 4 drachms.

Expressed from seeds of *Ricinus communis* (Euphorbiaceæ). Soluble about 1 in 3½ of alcohol 90%. Miscible with ether and glacial acetic acid. The seeds, but not the oil, contain the poisonous protein, ricin; the "press cake," therefore, is poisonous. The purgative action is due to the fatty acids, of which ricinoleic is a principal member.

*Pharmaceutical* oil, as distinct from soap-makers' and other industrial oil, does not deposit in cold weather.

**Ricin.** A vegetable toxin or toxalbumin, is tremendously potent. When small doses are injected hypodermically immunity is produced, antiricin being formed. This fact paved the way for the foundation of serum therapeutics. Ricin has two biological functions—one toxic, and the other antigenic. Potassium permanganate, hydrogen peroxide (30%), ozone, chlorine, bromine iodine and ultra-violet rays, all destroy the toxic properties without affecting the antigenic. Ricin partially oxidised by potassium permanganate, when injected into rabbits, develops in them so great an immunity against untreated ricin that after 2 or 3 weeks they are able to receive 100 to 120 times the normal lethal dose, and 0.25 ml. of serum from these rabbits protects mice against a fatal dose of ricin.

**Flavouring.** May be prescribed as *Oleum Ricini Aromaticum*, or with 2 dr. of *Tinctura Cardamomi Composita* to the ounce, or in capsules.

**Uses.** A mild but effectual purgative. Especially valuable in acute diarrhoea, particularly when due to food poisoning. Small repeated doses may be given in the intestinal colic of children. It is rendered more efficacious when mixed with an equal quantity of glycerin. Castor oil is a soothing application to the conjunctiva and allays irritation due to foreign bodies in the eye. It is also employed for making solutions of alkaloidal bases for ophthalmic purposes.

Prolonged inhalation of the vapour of castor oil produces a purgative effect. It is generally known among flying officers that the fumes from rotary engines using pure castor oil as a lubricant keep the bowels open.—G. G. Macphree, *Brit. med. J.*, ii/1934, 1045.

#### **Emulsio Olei Ricini Aromatici (B.P.C.).**

**Dose.**—1 to 2 ounces (30 to 60 ml.). Contains 30% v/v of aromatic castor oil.

#### **Enema Olei Ricini (B.P.C.).**

**Dose.**—20 ounces (600 ml.). 10% v/v in 5% w/v aqueous soft-soap solution. 20% v/v in mucilage of starch or olive oil is also used, in doses of 10 oz.

#### **Mistura Olei Ricini (B.P.C.).**

**Dose.**—1 to 2 ounces (30 to 60 ml.).

An emulsion containing 3 dr. of castor oil per oz.

#### **Oleum Ricini Aromaticum (B.P.C.).**

**Dose.**—1 to 8 drachms (4 to 30 ml.).

Castor oil flavoured with vanillin, saccharin, chloroform and oils of cinnamon, clove and pimento. Should be recently prepared.

**Unguentum Olei Ricini Compositum (L.H.).** *Syn.* BURN OINTMENT.

Zinc oxide 1, yellow soft paraffin 2, hydrous wool fat 2, castor oil 3.

**Magnesi Ricinoleas** **Dose.**—1 to 4 drachms (4 to 16 g.).

A white powder, employed as a solid form of castor oil in powders, or pills.

**Sodii Ricinoleas.** *Prop. Name.* SORICIN (*W. S. Merrell, Cincinnati; Squire, London*).

The sodium salt of ricinoleic acid. A powerful detoxifying agent. Solution in water suitably flavoured is used as a mouth wash, and a paste of sodium ricinoleate 1 and white soft paraffin 3 is used in dentistry.

**Uses.** Sodium ricinoleate lowers surface tension and adsorbs bacterial toxins. Is used as an antiseptic. For oral use in the

treatment of pyorrhœa, a 1 to 4% solution is used, the solution being syringed into pyorrhœal pockets and allowed to remain a few minutes. Is also of value in gingivitis and Vincent's angina.

The antiseptic activity, although marked is limited to certain bacteria. Intestinal bacilli are resistant to all soaps and are unaffected. Bacilli found in respiratory organs and in the buccal mucous membrane are susceptible. Meningococcus, Pfeiffer's bacillus, diphtheria bacillus, tubercle bacillus, and *Brucella abortus* are destroyed. Streptococci are rapidly killed but staphylococci are unaffected, as also are moulds and yeasts.—H. Violle, *C. R. Acad. Sci., Paris*, 1933, 197, 714.

**ACUTE GINGIVITIS.** Trichloroacetic acid as a strong caustic leaves the gums in a weakened condition and liable to further infection. Sodium ricinoleate is better—probably acts by adsorption into the toxin molecule. Apply 33% of yellow variety, or 9% of white to the dried sockets. Follow with hot potassium chlorate and carbolic mouth wash.—J. Wheatley, *per Pharm. J.*, ii/1931, 227.

**VARICOSE ULCERS** are treated by the injection of a 5% solution of sodium ricinoleate into the largest vein proximal to the ulcer. A culture from the ulcer should previously be obtained and a Wassermann test made. After the injection an elastic adhesive bandage is applied by the Dickson Wright method. After two weeks another injection is made and the bandage re-applied. The treatment is repeated if necessary after one month.—S. Gordon, *Canad. med. Ass. J.*, 1940, 4.

**VARICOSE VEINS.** In persons whose varicosities were resistant to other sclerosing agents, or which recurred after the administration of other sclerosing agents, an excellent end-result after the use of sodium ricinoleate, employing from 1 to 4 ml. of a 2% solution. Reactions and pain less than with other sclerosing solutions. Repeated injections of from 1 to 3 ml. at different levels of the varicose veins is preferable to the injection of a larger amount at one injection.—F. M. Postlethwaite, *per J. Amer. med. Ass.*, ii/1936, 1505.

**Jelopar (Research Products, London).** Nasal jelly containing sodium ricinoleate, menthol, hexylresorcin, rosettol and liquid and soft paraffin. In catarrh, etc. Lodynic is a preparation of similar composition for use as a nasal spray.

[P1] **Oleum Crotonis** (*B.P.C.*, *P. Helv. V*, *Fr. Cx.*). *Syn.* OLEUM TIGLII.

[P1] "*Croton, oil of.*"

**Dose.**— $\frac{1}{2}$  to 1 minim (0.03 to 0.06 ml.). *Fr. Cx.* gives max. during 24 hours 0.1 g. (= 2 minims nearly). Expressed from seeds of *Croton Tiglium* (Euphorbiaceæ). A yellow to brownish viscid liquid with nauseating odour and acrid taste.

**Soluble** in ether and in olive oil. Activity is due to croton-resin, a powerful irritant and vesicant.

**Antidotes.** Empty stomach by emetic or stomach tube. Keep patient lying down and warm. Give demulcent drinks freely. Stimulants, e.g., brandy  $\frac{1}{2}$  oz., or aromatic spirit of ammonia  $\frac{1}{4}$  dr., in water; spirit of camphor, 10 m. in milk, repeated. Tincture of opium by mouth to check the diarrhœa and relieve pain. Saline infusion.

**Uses.** The oil is a powerful skin irritant; it will blister and even cause suppuration and scarring. Internally it is so violent a purgative that it is rarely given except to lunatics for obstinate constipation, and in cases of apoplexy (1 or 2 drops placed on the back of the tongue). If used in this manner it must be diluted with sugar or butter to prevent local inflammation. It should never be given to children, pregnant women, or feeble subjects, and is contraindicated in the presence of hæmorrhoids and inflammatory conditions of the stomach and intestines.

[P1] **Linimentum Crotonis** (B.P.C.) contains 12% *v/v* of the oil with oil of cajuput and alcohol 90%.

Well diluted may stimulate growth of hair on bald patches. Also used as a counter-irritant, but may produce excessive inflammation.

**Oleum Elliott**, so-called to distinguish from croton oil, is obtained from the seeds of *Croton Elliottianus*. Dose.—1 to 3 minims, in capsules. A potent aperient.

## OPIUM

B.P., U.S.P. XI, Fr. Cx., etc.

Syn. GUM OPIUM, RAW OPIUM.

[D] "Raw Opium (see p. 1133); prepared opium (see p. 1133); medicinal opium."

NOTE.—The Dangerous Drugs Act, 1925, section 4 (1) defines medicinal opium as raw opium which has undergone the processes necessary to adapt it for medicinal use in accordance with the requirements of the British Pharmacopœia, whether it is in the form of powder or is granulated or is in any other form, and whether it is or is not mixed with neutral substances.

[P1] "Opium."

[S1] "Opium except substances containing less than 0.2% of morphine calculated as anhydrous morphine."

[S6] "Opium—specify the proportion of morphine contained in the preparation."

See also Morphine.

The inspissated juice obtained by incision of the capsules of *Papaver somniferum* (Papaveraceæ). Only the older pre-monopoly forms of the Turkey and European varieties are included in the B.P. description. Manipulated forms of Turkey, Yugoslavian and Bulgarian opium are now imported and are suited for pharmacy. Other varieties, including Iranian and Afghanistan, are used chiefly for morphine manufacture. Indian opium is still produced but is not now available in Great Britain.

The B.P. requires opium in its moist state, as imported, to contain not less than 9.5% of anhydrous morphine. When Opium is prescribed Opium Pulveratum must be dispensed. Fr. Cx. requires 10% of morphine on the drug dried at 60°. I.A. requires 10%. Opium (U.S.P. XI) in its normal moist condition contains not less than 9.5% of anhydrous morphine. The standards are extremely low, and opiums containing such small proportions would now be regarded as being of very inferior quality. A more reasonable minimum standard for the morphine content of raw opium would be 12%.

**Incompatible** with vegetable astringents, alkaline carbonates, salts of mercury, iron, lead and zinc.

**Antidotes.** Treat as for poisoning by morphine, see p. 697.

**Uses.** Opium has the same therapeutic indications (and contraindications) as morphine, but its action is exerted less rapidly owing to its slower absorption, and it is more liable to upset digestion and cause constipation. This constipating action, however, renders it of great value in the treatment of diarrhoea and for the relief of intestinal, biliary, and renal colic. Morphine has a more rapid and potent anodyne action than opium, and the latter is employed for the slighter degrees of pain and to induce sleep, though it should not be employed for chronic insomnia. On the other hand, opium is more diaphoretic than morphine and is of value in conjunction with ipecacuanha (as in Dover's powder) in the early stages of a cold. Dover's powder is also the ideal medicament for a dry useless cough, the opium depressing the cough reflex and the ipecacuanha acting as an expectorant.

Opium is used externally in the form of the liniment in rheumatism and neuralgia, and in the form of ointment or suppositories for rectal conditions, but it exerts no action on the peripheral nerve endings, and its use in this manner is irrational.

Opium addiction is seldom met with in this country, though it is common in the East; treatment is the same as for morphine addiction (*q.v.*).

[P1-81] **Emplastrum Opii** (*B.P.* 1898). 1 in 10 of resin plaster (*exempt* [D]). [P1-81] *Fr. Cx.* has opium extract 1, elemi 1, diachylon plaster with gum (*Fr. Cx.*) 2 (*exempt* [D]). For preparations of similar composition also *exempt* [D], see p. 1140.

[P1] **Enema Opii** (*B.P.C.*). *Dose.*—2 to 4 ounces (60 to 120 ml.). Tincture of opium 0.5 to 6% *v/v* in mucilage of starch.

[D-P1-81] **Extractum Opii Liquidum** (*B.P.C.*).

*Dose.*—5 to 30 minims (0.3 to 2 ml.).

Contains 0.75% *w/v* of morphine.

[D-P1-81] **Extractum Opii Siccum** (*B.P.*). *Syn.* EXTRACTUM OPII AQUOSUM (*I.A.*), EXTRACTUM OPII (*P. Austr.*, *P. Helv. V*, *P. Belg. IV*, *P. Hung.*, *P.G. VI*, *P. Ned. V*, *P. Ital. V*, *F.E. VIII*).

*Dose.*— $\frac{1}{4}$  to 1 grain (0.016 to 0.06 g.). 1 grain contains  $\frac{1}{2}$  grain of morphine. Standardised to 20% of morphine.

*Fr. Cx.* has a firm extract of similar strength with max. single dose  $1\frac{1}{2}$  grains; max. in 24 hours 5 grains approximately.

[P1] **Linctus Scillæ Compositus** (*B.P.C.*). *Syn.* LINCTUS SCILLÆ OPIATUS, GEE'S LINCTUS, LINCTUS CAMPHORÆ COMPOSITUS (*K.C.H.*, *P.E.H.C.* (not for children), *St. G.H.*), LINCTUS SEDATIVUS (*St. T.H.*). *Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Camphorated tincture of opium, oxymel of squill, and syrup of tolu, equal parts.

[P1] **Linctus Tolu cum Opio** (*Brompton H.*), Linctus Camphoræ Compositus (*L.H.*), and Linctus Scillæ et Tolu (*W.H.*), *syn.* LINCTUS SCILLÆ CO., use syrup of squill in place of oxymel in preceding.

[P1] **Linctus Opiatus** (*C.X.H.*). Tincture of opium 2 m., oxymel of squill 20 m., dilute sulphuric acid 5 m., treacle 20 m., water to 1 dr.



[P1] **Linctus Scillæ** (*St. M. H.*). Oxy-mel of squill  $\frac{1}{2}$  dr., camphorated tincture of opium 15 m., honey to 1 dr.

[P1] **Linctus Scillæ Compositus** (*U. C. H.*) contains oxy-mel of squill  $\frac{1}{2}$  dr., camphorated tincture of opium 10 m., tincture of ipecacuanha 5 m., mucilage of acacia to 1 dr.

[P1-81] **Linimentum Opii** (*B. P. C.*).

Tincture of opium 1, liniment of soap 1; filter after a few days (*exempt* [D]). For preparations of similar composition also *exempt* [D], see p. 1140.

[D-P1-81] **Liquor Opii Sedativus** (*B. P. C.*).

*Dose.*—5 to 30 minims (0.3 to 2 ml.).

Contains 1% *w/v* of anhydrous morphine, or about  $\frac{1}{2}$  grain in 30 minims.

[P1] **Mist. Acid. c. Opio** (*N. I. F.*).

Aromatic sulphuric acid 10 m., liquid extract of opium 5 m., water to  $\frac{1}{2}$  oz.

[P1] **Mistura Opii et Glycyrrhizæ Composita** (*U. S. P. XI*). *Syn.* BROWN MIXTURE. *Average dose.*—1 drachm (4 ml.).

Fluidextract of liquorice 12, potassium antimonyltartrate 0.024, camphorated tincture of opium 12, spirit of ethyl nitrite 3, glycerin 12, in water to 100.

[P1] **Mistura Sodæ cum Opio** (*St. M. H.*). Tincture of opium 3 m., dilute hydrocyanic acid 2 m., sodium bicarbonate 6 gr., water to 1 oz.

[D-P1-81] **Opium Pulveratum** (*B. P.*, *P. Belg. IV*, *P. Ital. V*, *P. Helv. V*). *Syn.* PULVIS OPII.

*Dose.*— $\frac{1}{2}$  to 3 grains (0.03 to 0.2 g.). 3 grains contains  $\frac{3}{10}$  grain of morphine.

Consists of opium dried at a moderate temperature, reduced to a fine or moderately fine powder and adjusted by the addition of lactose to contain 10% of anhydrous morphine.

*U. S. P. XI* includes **Opium Granulatum**, in No. 16 powder approx., and **Opium Pulveratum**, in very fine powder. Both contain 10 to 10.5% of anhydrous morphine.

[D-P1-81] **Pilulæ Saponis cum Opio** (*B. P. C.*). *Syn.* PILULÆ SAPONIS COMPOSITÆ. *Dose.*—1 or 2 pills.

Each pill contains  $\frac{2}{3}$  gr. of powdered opium and about 1 gr. of hard soap.

[P1-81] **Pulvis Cretæ Aromaticus cum Opio** (*B. P.*).

*Dose.*—10 to 60 grains (0.6 to 4 g.). 60 grains contains about  $\frac{1}{2}$  gr. of anhydrous morphine.

Contains opium 2½% in Pulvis Cretæ Aromaticus (*exempt* [D]). Tablets each contain 5 grains (0.3 g.).

[D-P1-81] **Pulvis Opii Compositus** (*B. P. C.*).

*Dose.*—5 to 15 grains (0.3 to 1 g.).

Contains 10% of powdered opium with black pepper, ginger, caraway and tragacanth.

*Note.* Pulvis Opii Compositus (*P. Ned. V*) is Dover's powder.

[P1] **Sirop Diacode** (*Fr. Cx.*) contains tincture of opium 1% *w/w* in simple syrup. [P1] **Sirop d'Opium** contains 5%.

[P1] **Syrupus Camphoræ Compositus** (*B. V. H.*). *Dose.*—1 teaspoonful, containing tincture of opium about 1 m., vinegar of ipecacuanha 3½ m., and vinegar of squill 1½ m.

Camphor 30 gr., oil of anise 30 m., benzoic acid 45 gr., glacial acetic acid 1½ oz., tincture of opium 2½ oz., vinegar of squill 10 oz., vinegar of ipecacuanha 10 oz., sucrose 7 lb., burnt sugar *q.s.*, water to 1 gallon.

**[D-P1-81] Tinctura Opii (B.P.).** *Syn.* LAUDANUM, TINCTURA THEBAICA.

*Dose.*—5 to 30 minims (0.3 to 2 ml.). 30 minims contains  $\frac{1}{4}$  grain of morphine.

Prepared by macerating opium in boiling distilled water to which alcohol is added after 6 hours. Contains 1% *w/v* of anhydrous morphine. *P. Ned. V*, *P. Hung.*, *P. Belg. IV* and *P. Ital. V* contain 1% of morphine, made with 70% alcohol. *P. Helv. V* is made with 5% of extract of opium, using 20 of alcohol 95% and 70 of water. *Fr. Cx.* and *F.E. VIII* dissolve 1 g. of opium extract in 19 g. of alcohol 70% to produce the same strength.—*Max. single dose* 35 minims; *max. during* 24 hours 110 minims approximately. *I.A.* requires 10% strength by percolation with alcohol 70% and 1% morphine.

**[D-P1-81] Tinctura Opii (U.S.P. XI).** *Syn.* TINCTURE OF DEODORIZED OPIUM. *Average dose.*—10 minims (0.6 ml.).

Granulated opium exhausted with water, the product evaporated, boiled for 15 minutes and allowed to stand overnight; the mixture is then heated to 80° and treated with hard paraffin; on cooling, the paraffin is removed and washed and the filtrate adjusted to volume with water, alcohol added and the product diluted with a mixture of alcohol and water so that the final tincture contains 1% of anhydrous morphine.

**[P1] Tinctura Anticholerica Conradi.** *Syn.* CONRAD'S KOLERADRABER.

*Dose.*—Over 20 years, 40 drops; over 5 years, 1 drop for each year. Must not be given to a child under 5 years.

Tincture of opium 1, tincture of cascarrilla and camphorated spirit of ether, of each 2, bitter tincture of rhubarb 5.

**[P1] Tinctura Thielemanni (P. Suec. X).** *Syn.* THIELEMANN'S KOLERA-DRABER. *Dose.*— $\frac{1}{4}$  drachm (2 ml.).

Oil of peppermint 3, alcohol 90% 22, tincture of opium with saffron 10, tincture of ipecacuanha 25, ethereal tincture of valerian 40.

**[P1] Tinctura Opii Ammoniata (B.P.C.).** *Syn.* SCOTCH PAREGORIC.

*Dose.*— $\frac{1}{4}$  to 1 drachm (2 to 4 ml.).

Contains 10% *v/v* of tincture of opium (equivalent to 0.1% of anhydrous morphine), 20% *v/v* of dilute solution of ammonia with oil of anise and benzoic acid. One ounce contains approximately  $\frac{1}{4}$  grain anhydrous morphine.

**[P1] Gasman's Drops.** *Liq. Ammon. Fort.* 10 m., *Tinct. Capsici* 10 m., *Tinct. Opium* 60 m., *Aq. Chlorof.* ad 8 oz.

**[P1] Tinctura Opii Camphorata (B.P.).** *Syn.* TINCTURA OPII BENZOICA (*I.A.*), TINCTURA CAMPHORÆ COMPOSITA, PAREGORIC, PAREGORIC ELIXIR, ELIXIR PARÉGORIQUE (*Fr. Cx.*).

*Dose.*— $\frac{1}{4}$  to 1 drachm (2 to 4 ml.). 1 drachm contains about  $\frac{3}{8}$  grain of anhydrous morphine.

Tincture of opium 5% *v/v*, with benzoic acid, camphor and oil of anise in alcohol (60%). Contains 0.05% *w/v* of morphine.

*Fr. Cx.*, *P.G. VI*, *P. Belg. IV*, *F.E. VIII*, and *P. Ned. V* have 0.05% of morphine, but amounts of the other ingredients differ. *P. Jap.* has 1 of opium in 200.

*Tinct. Camph. Co.* of the *Portuguese Pharmacopœia* is a **[D-P1-81]** liniment containing 20 times as much opium as the British tincture.

**[P1] Tinctura Opii Camphorata (U.S.P. XI).** *Average dose.*—60 minims (4 ml.).

Tincture of opium 4, oil of anise 0.4, benzoic acid 0.4, camphor 0.4, glycerin 4, in sufficient diluted alcohol to produce 100. Strength 0.035 to 0.045% *w/v*

of anhydrous morphine. It may also be prepared from powdered opium by a five-day maceration.

[P1] **Mist. Camph. Co. (N.I.F.).** Camphorated tincture of opium 15 m., strong solution of ammonium acetate 15 m., tincture of ipecacuanha 6 m., potassium nitrate 5 gr., ammonium carbonate  $1\frac{1}{2}$  gr., water to  $\frac{1}{2}$  oz.

[D-P1-81] **Tinctura Opii Crocata (B.P.C., I.A.).** *Syn.* SYDENHAM'S LAUDANUM. *Dose.*—5 to 30 minims (0.3 to 2 ml.).

Contains 1% w/v of anhydrous morphine (about  $\frac{1}{2}$  grain in 30 minims) with clove and cinnamon, and tinted with saffron.

*P.G. VI, F.E. VIII, P. Belg. IV, P. Ned. V, P. Helv. V, Fr. Cx.* approximate this.

[P1-81] **Tabellæ Pulveris Ipecacuanhæ et Opii (B.P.C.)** contain 5 gr. (0.3 g.) (*exempt [D]*). For tablets of similar composition also *exempt [D]*, see p. 1141.

[P1] **Trochisci Sedativi (T.H.)** contain  $\frac{1}{10}$  gr. of extract of opium with fruit basis.

[D-P1-81] **Vinum Opii Crocatum**, as used in Thielemann's Koleradraaber (*q.v.*), in Norway, has the composition:—Opium powder 15, cinnamon 1, clove 1, saffron 5, Malaga wine 150.

[D-P1-81] **Koptalgos (Duncan Flockhart, Edinburgh).** Denarcotised preparation of opium containing 0.375% of morphine. *Dose.*—5 to 40 m. in place of the tincture.

[D-P1-81] **Liquor Opii Sedativus "Battley" (Allen & Hanburys, London).** A liquid preparation of opium containing 1 gr. of anhydrous morphine per dr. *Dose.*—5 to 10 minims.

[D-P1-81] **Nepenthe (Ferris, Bristol).** A liquid preparation of opium containing 0.84% of anhydrous morphine (about 1 gr. in 130 minims).

[D-P1-81] **Somnigen (Heulett, London).** Dialysed solution of the hydrobromides of the alkaloids of opium in sherry, containing 0.75% w/v of anhydrous morphine. *Dose.*—5 to 40 m.

[D-P1-81] **Papaveretum (B.P.C.).** *Syn. and Prop. Names.* OPIUM CONCENTRATUM (*P.G. VI*), EXTRACTUM CONCENTRATUM OPII (*Fr. Cx.*).

*Dose.*— $\frac{1}{2}$  to  $\frac{1}{4}$  grain (0.01 to 0.02 g.);  $\frac{1}{12}$  to  $\frac{1}{8}$  grain (0.005 to 0.01 g.) by injection. *P.G. VI* has max. single dose  $\frac{1}{2}$  grain; max. in 24 hours  $1\frac{1}{2}$  grains.

The total or principal alkaloids of opium as hydrochlorides, adjusted to contain 50% morphine. *P.G. VI* gives elaborate instructions for preparation.

**Soluble** about 1 in 15 of water; less soluble in alcohol.

**Uses.** Papaveretum is less toxic than morphine and is better tolerated; it has a less depressant action on the respiratory centre, is less constipating and rarely causes vomiting. It has been recommended for use in place of opium, since it may be injected hypodermically, and it may be used in all cases in which morphine or opium is indicated.

[D-P1-81] **Tabellæ Papavereti (B.P.C.)** contain  $\frac{1}{2}$  gr. (0.01 g.).

[D-P1-81] **Hydrochlorates Alcaloideorum Principalium Opii (P. Ned. V).** *Syn.* OPIALUM, OPIAL. *Dose.*—Max. *per os* per diem 3 grains (0.2 g.), 2 grains (0.12 g.) by injection.

Contains narcaine hydrochloride 1, thebaine hydrochloride 2, codeine hydrochloride 2.5, papaverine hydrochloride 4, narcotine hydrochloride 30, morphine hydrochloride 50, and sodium chloride 10.5%.

[D-P1-81] **Opialum** (*P. Helv. V*) is similar, but contains 24·5% of narcotine hydrochloride and 66% of morphine hydrochloride, with no sodium chloride. There is less danger of toxic effects than from opium, as smaller quantities can be given.

Preferable to morphine as a sedative during first stage of labour. It may be administered orally or by injection in a dose of  $\frac{1}{4}$  gr., the injection being supplemented by 2 ml. of 50% solution of magnesium sulphate intramuscularly and repeated 2-hourly for two succeeding doses, according to Gwathmey's technique. Administration of morphine should be withheld until the cervix will admit three fingers, or the patient is not helped by potassium bromide and chloral hydrate.—L. McIlroy and H. Rodway, *J. Obstet. Gynec.*, 1933, 1175.

[D-P1-81] **Alopon** (*Allen & Hanburys, London*). Preparations of papaveretum available as powder, oral tablets (containing  $\frac{1}{4}$  gr.), solution (2%), ampoules ( $\frac{1}{4}$  or  $\frac{1}{2}$  gr. per ampoule) and hypodermic tablets ( $\frac{1}{4}$  gr.). Also supplied in ampoules with atropine or hyoscine.

[D-P1-81] **Omnopon** (*Roche Products, Welwyn Garden City*). Preparations of papaveretum available as powder, oral tablets (containing  $\frac{1}{4}$  gr.), hypodermic tablets ( $\frac{1}{4}$  gr.) ampoules ( $\frac{1}{4}$  gr. per ml.). Also supplied in ampoules with scopalamine in various strengths.

[D-P1-81] **Opioloid** (*Richter, London*). Tablets for oral use containing the alkaloids of opium, papaverine, codeine and  $\frac{1}{2}$  gr. morphine hydrochloride. *Dose*.—1 or 2 tablets as required. Narcotic and sedative.

[D-P1-81] **Opoidine** (*Macfarlan, London*) and [D-P1-81] **Pavopin** (*T. & H. Smith, London*) are also preparations of papaveretum available in tablets and ampoules.

[P1] **Papaveris Capsula** (*B.P.C., Fr. Cx., P. Helv. V*). *Syn.* POPPY HEADS.

*Note*.—Fleurs de Coquelicot in France = poppy petals.

The dried fruits of *Papaver somniferum* before dehiscence has occurred. For making galenicals, the seeds are removed.

[P1] **Decoctum Papaveris et Anthemidis Forte** (*B.P.C.*). *Syn.* DECOCTUM PAPAVERIS ET ANTHEMIDIS CONCENTRATUM.

Contains 25% each of chamomile and poppy capsule in alcohol and water. Diluted with hot water it is used as a fomentation in neuralgia, peri-dental abscesses and gum-boils.

[P1] **Extractum Papaveris Liquidum** (*B.P.C.*). *Syn.* LIQUOR PRO SYRUPU PAPAVERIS.

*Dose*.—10 to 30 minims (0·6 to 2 ml.).

Contains about 0·17% of anhydrous morphine or about  $\frac{1}{25}$  gr. in 30 m.

[P1] **Syrupus Papaveris** (*B.P.C.*).

*Dose*.— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Liquid extract of poppy capsule 1 in 8 with syrup. Contains about  $\frac{1}{25}$  gr. of morphine per drachm.

**Rhœados Petalum** (*B.P.C.*). *Syn.* RED-POPPY PETALS, COQUELICOT (*Fr. Cx.*). The fresh or dried petals of *Papaver Rhœas* (*Papaveracæ*).

**Syrupus Rhœados** (*B.P.C.*).

*Dose*.— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.). A solution of sucrose in an aqueous infusion of the dried petals. Used only as a colouring agent.

## OVOLECITHINUM

*B.P.C.*

*Syn.* LECITHIN (*P. Ned. V, F.E. VIII*).

*Dose*.—Internally 3 to 8 grains (0·2 to 0·5 g.) preferably half an hour before meals. This dose may well be increased if it is digested, as an average egg contains 16 gr. approx. Is usually administered as the elixir or in pills.

Subcutaneously  $\frac{3}{4}$  to 2 grains (0.05 to 0.12 g.) in sterile olive oil every second day.

A yellowish wax-like mass prepared from egg yolks by extraction with alcohol or ethyl acetate. When pure it consists of choline distearyl glycerophosphate, and is broken up by the pancreatic juice into glycerophosphoric acid, fatty acids and choline. It is a constituent of the brain 11%, and of yolk of egg 7%; milk (human, cows', etc.) contains varying amounts.

**Soluble** 1 in 30 of alcohol 90%, 1 in 5 of ether, and in chloroform, benzene, carbon disulphide and fatty oils. It combines with certain metals, e.g., copper.

**Uses.** Has been given in neurasthenia, various nervous diseases, diabetes, marasmus, tuberculosis, tabes and general paralysis, and in all diseases producing a disturbance of nutrition. It has also been employed in the withdrawal treatment of opium and morphine addiction (see p. 700). It is said to cause a marked increase in patient's weight, to improve the general well-being, and to augment the blood corpuscles, but since the ordinary diet furnishes an ample supply of lecithin and other phosphorus compounds, it is difficult to see how the small quantities employed can have any other than a psychic effect.

**Elixir Ovocleithini (B.P.C.).** *Syn.* ELIXIR LECITHINI.

**Dose.**—1 to 4 drachms (4 to 16 ml.), half an hour before meals.

Contains 1 gr. of ovocleithin per dr. in a lemon-flavoured basis.

**Enema Ovi (B.P.C.).**

**Dose.**—4 ounces (120 ml.). 1 or 2 yolks of egg in peptonised beef tea.

[P1-S1] **Pilulæ Ovocleithini (B.P.C.).** *Syn.* PILULÆ LECITHINI.

**Dose.**—1 to 4 pills. Contain  $\frac{1}{80}$  gr. of strychnine and  $1\frac{1}{2}$  gr. of ovocleithin.

**Bromlecithin (Richter, London).** Described as a natural lecithin, containing 20% of bromine in tablets of  $\frac{1}{4}$  gr. and  $\frac{4}{3}$  gr. For anæmia, neurasthenia and hysteria. **Dose.**—1 to 2 tablets twice daily. **Iodolecithin** is a similar compound with 20% of iodine in place of bromine, in 4 gr. tablets and  $1\frac{1}{2}$  gr. pills for arteriosclerosis, rickets and asthma. **Dose.**—1 tablet or 1 to 2 pills thrice daily.

**Lecithinol (Richter, London).** Emulsion of lecithin in ampoules, for administration in neurasthenia and malnutrition. **Dose.**—1 ml. injected 3 or 4 times weekly.

## OXYGENIUM

B.P., U.S.P. XI, Fr. Cx.

O = 16.000.

Oxygen is obtained commercially by the rectification of liquid air by a process of fractional liquefaction, or by the electrolysis of water. It is of not less than 98% purity, and is sold compressed in cylinders, a common size containing the equivalent of 20 cubic feet (560 litres approximately).

**Administration.** Oxygen is administered in various ways, the most efficient but more elaborate methods being the "oxygen

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chamber" and the "oxygen tent." A simpler method is the use of a mask or a nasal catheter, the gas being bubbled through hot water. Metal cylinders containing compressed oxygen should be fitted with a suitable reducing valve by which the rate of flow of the oxygen can be easily controlled. To avoid the possibility of explosion it is important that the reducing valve should be free from all traces of oil, and if the valve is of the rubber bellows type the tap of the reducer should always be opened before opening the main oxygen tap on the cylinder.

**Uses.** Oxygen inhalation is of great service in the treatment of anoxæmia, as in pneumonia, pulmonary œdema, anæmia, carbon monoxide poisoning, and the poisoning due to lung-irritant gases such as phosgene and chlorine. It is also of great value in respiratory failure due to post-operative pulmonary complications, and for resuscitation after partial drowning. Oxygen has little effect on the dyspnœa of cardiac disease or nephritis, but has been found of value in the treatment of emphysema and for the temporary relief of asthmatic attacks; in the latter condition it has recently been successfully employed in association with helium.

In acute anoxæmia the oxygen may be administered undiluted, but for continuous inhalation over long periods, as in pneumonia, the concentration should be maintained at about 50%, and never above 60%. The addition of 1% or more of carbon dioxide to oxygen stimulates the respiratory centre and causes deeper breathing, and such mixtures are often used for this reason; generally speaking, concentrations of carbon dioxide of 5% or more are dangerous, though they have been employed with beneficial effect in the treatment of coal-gas poisoning and post-operative collapse.

In congenital heart disease oxygen is of no avail; not indicated in cyanosis of cardiac origin, when lungs are comparatively clear. Chronic cyanosis of emphysema is temporarily relieved. Specially called for in acute pulmonary failure, together with inadequate ability for compensation by the heart and blood. Should be administered over hours or days.—*Per J. Amer. med. Ass.*, ii/1925, 1430.

Indications for oxygen therapy.—W. T. Richie, *Brit. med. J.*, ii/1927, 915.

Oxygen therapy.—W. M. Boothby (Council on Physical Therapy, A.M.A.), *J. Amer. med. Ass.*, ii/1932, 2026, 2106.

MIGRAINE. Severe migraine attacks are relieved within an hour or two by the inhalation of pure oxygen.—W. C. Alvarez, *Proc. Mayo Clin.*, 1939, 173.

**Helium and Oxygen.** Helium is an inert gas with a molecular weight of 4. Owing to its lightness it has a very high rate of diffusion, and if the nitrogen in the air is replaced with helium more oxygen is carried by the resultant mixture, which has an inherent mobility three times that of the air. In practice the mixture has proved of value in cases of intractable asthma and status asthmaticus, when oxygen alone was of no avail; it is also efficient in other obstructive lesions of the respiratory tract, especially in cases of post-operative or traumatic œdema of the larynx, and of transient paralysis of the vocal cords.

Since helium is an inert gas, it is important in practice to use cylinders containing a mixture of 20% oxygen and 80% helium, rather than have the gases separate; if separate cylinders are used

the helium may be turned on first and the patient asphyxiated before the oxygen is given.

**ASTHMA.** A mixture consisting of about  $\frac{1}{2}$  oxygen and  $\frac{1}{2}$  helium, administered by means of an air-tight oxygen tent with a specially designed hood just large enough for the head, is of definite value in relieving patients with severe intractable asthma. In status asthmaticus it can be life-saving. Its use may also be warranted in cases in which respiratory difficulty is so great that the cyanosis is not relieved by administration of 80% oxygen and 20% nitrogen. No ill-effects noted—one patient inhaled helium for nearly 24 hours continuously, and subsequently at intervals of 3 days. Effectiveness of helium believed due to its rapid diffusion.—C. K. Maytum, L. E. Prickman and W. M. Boothby, *Proc. Mayo Clin.*, 1935, 788.

In status asthmaticus the treatment may result in the saving of life; in severe, more or less continuous asthma, it produces an amelioration of the disease with recovery of complete sensitiveness to adrenaline in patients who previously had become refractory to it. In obstruction of the pulmonary airway from the bronchiole to the pharynx, inhalation of helium with oxygen lessens the respiratory effort and aids ventilation of the lungs in some instances thereby averting tracheotomy.—A. L. Barach, *J. Amer. med. Ass.*, ii/1936, 1278.

An artificial atmosphere of normal oxygen content (21%), but with 79% of helium replacing the normal nitrogen, is only one-third as heavy as ordinary air, and is about twice as easy to breathe. The mixture should be of great value in cases of respiratory obstruction, or in cases in which it is essential to economise muscular effort.—W. S. Sykes and R. C. Lawrence, *Brit. med. J.*, ii/1938, 448.

Helium and oxygen is a most valuable aid in terminating prolonged severe asthma when other methods fail to give relief, and it is of definite value in the treatment of other obstructive lesions of the respiratory tract.—C. K. Maytum, *Proc. Mayo Clin.*, 1938, 788.

**Injection of Oxygen.** Oxygen has been given by injection by various routes—intravenous, intraperitoneal, rectal and subcutaneous. *Subcutaneously*, it has been given in sciatica in doses of 250 to 400 ml., injected deeply, and in asphyxia, pneumonia, hæmoptysis and tuberculosis. *Intraperitoneal injections* are of value in tubercular diarrhoea, tubercular peritonitis and "tabes mesenterica." *Rectal injections* are of value in certain types of colitis. Growth of anaerobic bacteria is inhibited and the injured mucous membrane benefited.

Preferential site for injections is the outer border of the anterior surface of the thigh, three inches above the upper border of the patella. 150 to 500 ml. satisfactory. Valuable in neo-natal asphyxia, drowning, suffocation, carbon monoxide poisoning, lobar pneumonia, pleurisy, pulmonary tuberculosis, cardiac asthma, collapse due to hæmorrhage, and as a prophylactic of post-operative shock (500 ml. being injected at full pressure in 1 minute).—D. C. Welsh, *Brit. med. J.*, ii/1932, 147.

**HÆMOPHTYSIS.** Brilliant results in 80% of 50 cases following injection of 600 to 1000 ml. subcutaneously (site of injection not important).—A. Latinne, *Brux. méd.*, 1934, 219.

Tubercular hæmoptysis treated by oxygen injected subcutaneously, 500 to 600 ml. under the skin of the chest, if possible on the affected side. In 12 out of 20 cases hæmorrhage stopped at once, and in 4 after the injection had been repeated daily for 3 or 4 days.—A. Courcoux, per *Med. Annu.*, 1935, 453. Site of injection not important (may be given under skin of thigh), and smaller doses, e.g., 200 ml., are sufficient.—Pierre-Bourgeois, *ibid.*

**PNEUMONIA.** In pneumonia, as a preventive of chloroform or post-anæsthetic sickness, and in extensive burns and scalds. If sufficient is given to inflate an area of skin equal in size to the palms of two hands, the amount given is roughly 200 ml. In bad cases give at least 400 ml. and repeat in 6 hours if absorbed. The gas need not be heated or filtered, does not produce or aggravate lung trouble or cause local or general bad effects. Inject below and outside the nipple or breast.—T. S. Kirk, *Brit. med. J.*, ii/1928, 195.

**PULMONARY TUBERCULOSIS.** The injections, at a dosage of 200 ml. per injection, are given in the subcutaneous tissues of the anterolateral region of the thigh with an apparatus such as is commonly used for the performance of pneumothorax. The injections should be given slowly, and should be repeated every other day for about a month. The treatment results in disappearance of fever, increase of the blood pressure, improvement of the blood picture, formation of a greater number of erythrocytes and amelioration of the disease.—E. Frola, per *J. Amer. med. Ass.*, i/1936, 1430.

**SCIATICA.** The subcutaneous injection of oxygen affords a simple, painless and extraordinarily successful method for the relief of pain (and even for the complete cure) of acute and chronic sciatica. The method employed is as follows:—Connect by sterilised rubber tubing a cylinder of oxygen with fine adjustment to a sterile Record needle about  $\frac{1}{2}$  mm. in diameter and 2 inches long, *via* a bottle containing warm water. When the gas is bubbling gently through the bottle the needle is introduced into the subcutaneous tissue at the back of the thigh, in the line of the sciatic nerve, just below the gluteal fold. The needle is introduced an inch or more, care being taken that it does not penetrate muscle, but remains confined to the cellular tissue. The subcutaneous tissue of the thigh quickly “balloons” with gas, and when the skin is sufficiently tense the needle may be removed. The emphysema subsides fairly soon and will have disappeared in 48 hours, when another injection should be made lower down in the middle line of the thigh over the sciatic nerve. If necessary a third injection may be given just above the popliteal space. If care is taken to inject into the subcutaneous tissues only, complete relief of pain may be expected.—H. H. Brown, *Brit. med. J.*, ii/1938, 1390.

**Nitrogen.** N = 14.008. Nitrogen is a colourless, odourless, tasteless gas constituting about 77% by weight (79% by volume) of the atmosphere. Nitrogen prepared from the atmosphere contains a small amount of argon and other rare gases.

**ARTIFICIAL PNEUMOTHORAX.** This consists in introducing nitrogen or sterile air between the two layers of the pleura through a special needle, and thus inducing collapse of the lung. There is no chosen spot for the puncture—it is commonly made in one of the axillary lines in the seventh or eighth intercostal space. The aim is to find a spot where the lung is healthiest and to avoid the neighbourhood of cavities. A hypodermic injection of morphine is given  $\frac{1}{2}$  hour before the operation. A local anæsthetic such as 2% procaine hydrochloride is given to anæsthetise the body tissues down to the pleura.

The quantity of nitrogen or air injected is 200 to 300 ml. The intrapleural pressure and the amount of air introduced is recorded and at first the injections have to be repeated every two or three days. Later, the intervals between injections are increased to a fortnight or more and it is generally advisable to continue treatment for two or three years. X-ray control at frequent intervals is essential. The treatment is only applicable in carefully selected cases (estimated at about 5% of the total) and the best results are obtained in early cases of unilateral disease.

The young adult with a unilateral lesion and no tubercle bacilli in the sputum, the young adult with slight early infiltration without cavitation, with good general condition and normal blood picture and who is ambulant and afebrile, the man over 45 with slight fresh infiltration superimposed on an old fibroid tuberculosis, and a patient with bilateral disease and low resistance—are all examples of cases in which routine treatment, including rest, is indicated. Artificial pneumothorax is not in itself a cure for tuberculosis any more than a splint heals a broken leg. It is a means for putting a body with a diseased lung into a favourable condition to develop healing and powers of natural resistance. Beneficial as are its results



it demands expert technique, careful selection of cases and careful study of the individual patient.—*Rep. med. Offr. Minist. Hlth, Lond.*, 1933, 134.

Indications and contraindications.—L. S. T. Burrell, *Practitioner*, ii/1933, 392.

Highly satisfactory in the treatment of tuberculosis of the larynx. Of 35 cases, 24 were clinically cured or improved, in 6 the condition remained stationary and in 5 became worse.—R. Scott Stevenson, *Brit. med. J.*, ii/1933, 962.

In lobar pneumonia a pneumothorax should be produced as early as possible. 400 to 500 ml. usually given with ease, and two injections suffice in most cases, given at an interval of 24 hours. Striking relief of pain and dyspnoea, but severity and not course of disease altered.—A. Behrend and R. B. G. Cowper, *J. Amer. med. Ass.*, i/1934, 1907.

Though there has not yet been put forward absolute statistical proof that artificial pneumothorax or collapse therapy in general is very greatly superior to other methods of treatment, there is evidence accumulating gradually which points fairly clearly in this direction. The proportion of patients to whom treatment is applicable in its widest aspect, that is where completely efficient treatment can be instituted and where a good ultimate prognosis can be guaranteed, is not in an industrial community at present more than 5%. There are, however, very considerable numbers where the treatment is of temporary value, and where it may initiate the process of healing.—R. J. Peters, *Edinb. med. J.*, 1937, 276.

### **Nitrogenii Monoxidum (B.P., U.S.P. XI, Fr. Cx.).**

*Syn.* NITROUS OXIDE, LAUGHING GAS.  $N_2O = 44.02$ .

A colourless gas with characteristic odour and faintly sweetish taste. Soluble 1 in 2 (by volume) of water at ordinary temperatures.

Prepared by heating ammonium nitrate to about  $180^\circ$  when it splits up into nitrous oxide and water vapour.

The gas is passed through a strong solution of ferrous sulphate to remove nitric oxide—the traces of acid being removed by passing through alkali.

**Antidotes** (for treatment if dangerous symptoms arise during inhalation of nitrous oxide). Pull out tongue with forceps and insert finger into mouth to make sure that it is free from obstruction and to remove mucus. Extend the head and push the jaw forward. Give the patient fresh air, loosen clothing, and if patient is upright place in a recumbent position. Flap the face and chest with the end of a wet towel. Apply artificial respiration and administer a mixture of oxygen and carbon dioxide. Inject stimulants, such as nikethamide and strychnine.

**Contraindications.** The use of *pure* nitrous oxide is contraindicated in cases in which an asphyxial element already exists, *e.g.*, patients suffering from tumours or inflammatory swellings in the neck, and in cases which will be aggravated by a sudden rise of blood pressure, *e.g.*, patients with a dilated right heart, or those suffering from an aneurysm, or from extensive arteriosclerosis with high blood pressure.

**Uses.** Nitrous oxide is employed as an anæsthetic in minor surgery, in conjunction with oxygen as a general anæsthetic for major surgery and obstetrics, and for the induction of anaesthesia prior to maintenance with ether. Its advantages are that it is non-irritant, non-toxic, rapid in action, and recovery is equally rapid. Disadvantages are that unless oxygen or air is given, asphyxia occurs, while its effect is greatly reduced if more than minimal amounts of oxygen are admitted, muscular relaxation is

poor, and blood pressure is increased. As ordinarily administered *per se*, e.g., for dental extractions, anæsthesia is complete in about  $\frac{1}{2}$  minute, lasts for 20 to 40 seconds and recovery is usually complete in 2 to 3 minutes. Nitrous oxide is administered by means of a bag into which the gas is led from the cylinders, the bag communicating with the face-mask through a valve by which the expired gas is passed out into the air. Various forms of apparatus are also available by which the gas may be administered intranasally.

**Nitrous Oxide and Oxygen** is used for minor operations, lasting from 5 to 15 minutes, and operations which do not demand a great degree of muscular relaxation, also in operations on patients suffering from severe shock or from acute sepsis. Its use is not advisable with children. Preliminary medication with hypnotics is utilised, since a higher proportion of oxygen may then be employed. Pure nitrous oxide is administered at first, oxygen being admitted after induction as required to prevent anoxæmia while maintaining a sufficient depth of anæsthesia. Anæsthesia with gas-oxygen is frequently supplemented by the administration of very small amounts of ether. With this addition heavy pre-operative medication may be avoided, thus lessening the risk of respiratory failure.

For operations on regions other than the mouth or nose, injections of atropine  $\frac{1}{16}$  to  $\frac{1}{8}$  gr., morphine  $\frac{1}{2}$  to 1 gr., are given hypodermically  $1\frac{1}{2}$  or even 2 hours before the inhalation. Crile and others add scopolamine  $\frac{1}{16}$  to  $\frac{1}{8}$  grain. At first nitrous oxide with 2% oxygen is given with a pressure of 4 to 40 mm. of mercury. More or less oxygen is given according to circumstances—more if patient is cyanosed, less if he struggles. Unconquerable rigidity is controlled by giving ether—this may occur in about 10% of cases.—D. W. Buxton's *Anæsthetics*, 6th Edition.

During the second stage of labour, nitrous oxide gas and oxygen (ideal proportions 80 and 20%, but oxygen increased if co-operation is not good), administered by Boyle's or McKesson's portable apparatus, appear to give the best results. Duration, strength and frequency of uterine contraction increased rather than diminished in over 50% of cases investigated, and no instance of post-partum hæmorrhage. Administration of anæsthetic continued for half to three-quarters of a minute after each pain has ceased. During birth of the head chloroform should be added, but should be regarded only as an adjunct to nitrous oxide, and only used in sufficient quantity to relieve pain at the most acute stage.—L. McIlroy and H. Rodway, *J. Obst. Gynec.*, 1933, 1175.

The best modern anæsthetic. Best administered by the McKesson apparatus, without the use of ether or chloroform, and preceded by Omnopon and scopolamine as premedication. Ensures complete absence of psychic shock, is not followed by vomiting and does not aggravate any pathological condition present.—R. Jarman, *Brit. med. J.*, i/1934, 799.

## PANCREAS

The pancreas used as a source of medicinal products is the sweetbread of animals commonly used for food, and is generally obtained from the pig or the ox. It produces an external secretion or pancreatic juice, yielding enzymes which take part in digestive processes and reach the intestine along the pancreatic duct. Pancreatin is a mixture of these enzymes prepared from the pancreas by maceration with alcohol. The pancreas also contains small groups of cells or "islets of Langerhans," yielding the internal

secretion, and from which insulin is manufactured. In addition to insulin, recent work goes to show that there is a second internal secretion, which has been given the name "Lipocaic," and which is stated to be the active substance in pancreas responsible for the utilisation of fat.

The pancreatic juice contains several digestive ferments:—Trypsin, a proteolytic enzyme acting in an alkaline medium, converting protein, *e.g.*, casein of milk and fibrin, into peptones; amylase (amyllopsin) or pancreatic diastase which converts starch into dextrin, maltose and dextrose; lipase (steapsin), a lipolytic enzyme (emulsifies fats); and possibly the milk-curdling enzyme, rennin, converting casein into a form of peptone.

For invalids, aged persons, and those suffering from weak digestion, or those prostrated by fever or exhaustion, preparations of the pancreas may be employed, by means of which food may be partially or wholly digested previous to administration; their nutrition is thus maintained, and the stomach has time to regain its powers of digestion.

**GRAVES' DISEASE.** A simple and effective treatment consists in the administration of pancreatic extract (whole gland) thrice daily before food. Over-medication with iodine is to be deprecated, and in some successfully treated cases little or no iodine was given.—C. B. Macdonald, *Brit. med. J.*, ii/1937, 660.

**Lipocaic.** The depancreatized animal suffers from two known deficiencies, *i.e.*, of insulin and pancreatic juice. The fact that the adequate administration of insulin does not permit these animals to survive for long suggests that pancreatic juice may also be essential. It has been found, however, that the oral administration of fresh active pancreatic juice, together with insulin therapy, does not prolong life or prevent the characteristic fatty changes in the liver, but that these changes are prevented and the animals permitted to survive by the addition of raw pancreas to the diet. It was further shown that the choline or lecithin in pancreas could not account for this effect. The evidence seems to warrant that the active substance in pancreas responsible for the utilisation of fat, is other than choline and that it is specific and active in small amount. This internal secretion has been named *lipocaic*. It has been possible to secure an extract from the pancreas which exerts the typical effect of the gland in a daily dose of from 60 to 100 mg. of dry substance. This material is free of fat and contains not more than from 1 to 2% of free choline, and is effective both orally and subcutaneously. There is considerable evidence at present that the patient with diabetes mellitus is not returned to an entirely normal state by the administration of insulin. In particular he seems to suffer from a lessened capacity to utilise fats. It is definitely established that the diabetic patient, whether adequately treated or not, is much more liable to develop presenile atheromatosis and arteriosclerosis than the normal individual, and it has been said that the diabetic, who in the pre-insulin days used to die of acidosis, now dies from coronary disease or diabetic gangrene. Does this mean that many diabetic patients suffer not only from an insulin deficiency, but also from a deficiency of lipocaic, which manifests itself in a disturbance of fat utilisation, with deposition of fat in the liver and, in the more chronic cases, in the subendothelial layers of the arteries? Animal experiments suggest that this is the case.—L. R. Dragstedt, *J. Amer. med. Ass.*, i/1940, 29.

**Angioxyl (Roussel Laboratories, London).** An insulin-free pancreatic extract in 2 ml. ampoules containing 20 "hypotensive units." A vasodilator for use in the treatment of angina pectoris, Raynaud's disease, etc. *Dose*.—2 to 3 ampoules daily, by intramuscular injection. A syrup for oral administration is also available containing 4 hypotensive units per ml., for the treatment of mild vascular disturbances. *Dose*.—3 to 4 teaspoonfuls daily between meals.

**Tissue Extract No. 568 (Sharp & Dohme, London).** An insulin-free extract of the pancreas, with activity expressed in terms of units defined by its neutralising power against the pressor effect of adrenaline. Supplied in vials of 10 ml. (10 units per ml.). It has a vasodilator effect and is recommended for use in angina pectoris and related angiospastic conditions.

**Pancreatinum** (*B.P.*, *U.S.P. XI*, *Fr. Cx.*).

*Dose.*—3 to 10 grains (0.2 to 0.6 g.). *U.S.P. XI* average dose 8 grains. It should be given 2 to 3 hours after a meal to prevent its destruction by gastric acid, preferably with sodium bicarbonate.

A white or buff-coloured powder containing the enzymes trypsin, lipase and amylase, in respect of each of which the *B.P.* specifies a minimum standard of activity. It digests albuminoids and converts, if of *U.S.P.* standard, not less than 25 times its weight of starch into soluble carbohydrate.

It differs from pepsin in the rapid destruction of its proteolytic activity in the presence of acid.

*Soluble* in water, giving a turbid solution. Insoluble in alcohol 90% and in ether.

*Incompatible* with acids, caustic alkalis, tannin and astringent substances.

*Uses.* Aids the digestion of starch and protein, acting best in nearly neutral solution. Its activity is destroyed when solutions containing it are heated above 60°. Is used mainly for the preparation of pre-digested or peptonised foods (*vide infra*).

In chronic pancreatitis, pancreatin in suitable intestinal medication may be employed with advantage before the operation and also in cases unsuitable for operations. It has also been employed with success in sprue.

**Enema Pancreatini** (*B.P.C.*).

*Dose.*—4 ounces (120 ml.). Solution of pancreatin 6.5% *v/v* in equal parts of milk and beef tea.

**Glycerinum Pancreatini** (*B.P.C.*).

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.). 1 in 10.

**Liquor Pancreatini** (*B.P.C.*). *Syn.* LIQUOR PANCREATIS.

*Dose.*— $\frac{1}{2}$  to 2 drachms (2 to 8 ml.).

Contains 16 $\frac{1}{2}$ % *v/v* of glycerin of pancreatin with sodium bicarbonate in a diluted alcohol-glycerin solution.

**Pulvis Pancreatini Compositus** (*B.P.C.*). *Syn.* PULVIS PANCREATICUS, PEPTONISING POWDER.

Pancreatin 1, sodium bicarbonate 4.

**Peptone Pancreatique** (*Fr. Cx.*). A mixture of amino acids and polypeptides obtained by submitting beef to pancreatic digestion for 6 hours. It is usually in the form of a yellowish-white powder, soluble in water, insoluble in strong alcohol.

**Peptonised Milk.** To 25 gr. of compound pancreatin powder 5 oz. of tepid water is added, and then 1 pint of milk at 38°. The mixture is maintained at 38° for 15 minutes and then boiled to destroy the enzymes. Gruel, arrowroot, etc., may also be pre-digested in the same way. In the place of the water  $\frac{1}{2}$  pint of lime water may be used to the pint of milk. The preparation, if desired for early use, may be kept at 15° for 3 or 4 hours; it need not necessarily be boiled.

Peptonised milk is useful in gastric ulcer, intestinal catarrh, for infants' use generally, and in all forms of weakened digestive functions.

**Peptonised Beef Tea** is made by simmering  $\frac{1}{2}$  lb. minced meat with 1 pint of water containing a small quantity of sodium bicarbonate for 2 hours. The cooled mixture is treated with 25 gr. of compound pancreatin powder, set aside in a warm place, boiled and strained.

**Peptonised Beef Jelly and Chicken Jelly** (*Benger's Food, Manchester*). As a restorative, either may be taken alone by teaspoonful or dissolve 2 or 3 tea-

spoonfuls in a teacupful of boiling water (with pepper and salt). Enriches beef tea, soups, broths, etc. They are readily assimilated by weak digestions. Containing much of the flesh-forming elements of the meat in soluble form these peptonised preparations are superior to non-peptonised extracts.

**Tabellæ Pancreatini** (*B.P.C.*), *syn.* PEPTONISING TABLETS, contain pancreatin  $2\frac{1}{2}$  gr. and sodium bicarbonate 10 gr.

**Trypsinum** (*B.P.C.*).

*Dose.*—3 to 10 grains (0.2 to 0.6 g.).

Trypsin is stated to be produced simultaneously with amylase, and from the same cells in the pancreas. This enzyme is prepared commercially in the form of whitish or yellowish powder, possessing an odour like that of pepsin.

It converts all soluble and many insoluble proteins into amino-acids and polypeptides. Its activity may be determined by the *B.P.* method for trypsin in pancreatin. It is 4 or 5 times as active as pancreatin. The activity is destroyed in general at 100°.

*Soluble* slightly in water, more so in glycerin.

*Uses.* It assists digestion in diabetes, and it is occasionally employed for peptonising milk. More usually it is administered as pancreatin.

**Dipankrin** (*Richter, London*). Active principles of pancreas and duodenum. *Dose.*—1 or 2 tablets thrice daily. In pancreatic deficiency.

**Festan** (*Bayer Products, London*). Preparation of pancreatic enzymes consisting of lipase, amylase, protease and hemicellulase in enteric-coated pellets. *Dose.*—1 pellet thrice daily after meals. Dyspepsia due to fermentative insufficiency.

**Liquor Pancreaticus** (*Benger*) (*Benger's Food, Manchester*). *Dose.*—1 to 2 drachms (4 to 8 ml.) in water with meals or in farinaceous gruel, when cool enough to sip to aid intestinal digestion. As an addition to nutritive enemata, a dessertspoonful should be added to beef tea or milk-gruel just before its administration. Will not keep diluted, and presence of acidity or heating over 140°F. destroys the ferment.

**Liquor Trypsini Compositus** (*Allen & Hanburys, London*). A solution of the tryptic and amylolytic ferments of the pancreas for oral use. *Dose.*—1 or 2 teaspoonfuls three times daily.

**Lobulina** (*Napp, London*). Tablets containing extracts of pancreas and yeast for oral administration in diabetes mellitus. *Dose.*—2 to 4 tablets after the principal meals.

**Panacoids** (*Reed & Carnrick, Jersey City; Coates & Cooper, London*). Tablets containing desiccated pancreas 2 gr. and desiccated duodenal substance 1 gr. Intestinal indigestion and disorders of the pancreas.

**Pancrepatine** (*Anglo-French Drug Co., London*). Combination of a special extract of the pancreas and hepatic extract in "globules" containing 0.25 g. for the oral treatment of diabetes. [P1] **Pancrepatine Compound** contains in addition 0.05 g. of phenazone and 0.002 g. sodium methylarsenate in each globule.

[P1-87] **Panlittol** (*Armour, London*). Tablets containing pancreas  $2\frac{1}{2}$  grains, thyroid *B.P.*  $\frac{1}{10}$  grain. Hypertension.

**Panopsin** (*Endocrines-Spicer, Watford*). Tablets contain  $2\frac{1}{2}$  gr. of pancreatic amylpsin. For digestive disorders.

**Panterior Tablets** (*Parke, Davis, London*). Enteric-coated tablets each containing 5 gr. of triple strength pancreatin equivalent to 15 gr. of pancreatin *B.P.* *Dose.*—1 to 2 tablets after each meal. To assist pancreatic digestion. **Panterior Compound Tablets** contain triple strength pancreatin with sodium glycocholate and sodium taurocholate.

**Zymine** (*Fairchild, Bros. & Foster, New York; Burroughs Wellcome, London*). Extract of pancreas containing trypsin, pancreatic diastase and lipase and other enzymes. *Dose.*—1 to 6 gr. twice or thrice daily after food.

**PAPAINUM***B.P.C., Fr. Cx.*

*Dose.*—2 to 10 grains (0.12 to 0.6 g.).

A proteolytic enzyme occurring as a whitish or light brown amorphous powder, prepared from the juice of the papaw, the unripe fruit of *Carica Papaya* (Passifloraceæ).

Papaw fruit, fresh, divested of its seeds, in shape like a vegetable marrow, is a refreshing dessert fruit, with flavour something like the melon.

The enzyme has a wider range of activity, both with regard to pH and temperature, and is more difficult to destroy than either trypsin or pepsin. Its optimal temperature zone is above that favourable to bacteria, and it can therefore be used for long periods of digestion without bacterial contamination. A digest media prepared from papain can be used for preparation of diphtheria toxin.—A. F. Watson, R. A. Jaggart, and H. F. Mannion, *Quart. J. Pharm.*, 1938, 391.

*Isolation and Properties of Crystalline Papain.* Crystalline papain was prepared from papaya latex by precipitation successively with different amounts of ammonium sulphate and sodium chloride at suitable pH in the presence of sodium cyanide. Crystalline papain was obtained in the form of thin needles which changed on standing in contact with water for several months into large plates, having elongated hexagonal faces. It was slightly soluble in dilute salt solution, but soluble in alcohol (70%). Its isoelectric point was about pH 9.—A. K. Balls and H. Lineweaver, *J. biol. Chem.*, 1939, 130, 669.

*Uses.* As a digestive in chronic cases of dyspepsia with acid eructations and painful gastric fermentation. It acts in acid, alkaline or neutral media, and like pepsin, has the property of digesting fibrin (as much as 200 times its weight in some cases). Like rennet, it has the property of curdling milk and might be used as a substitute for it. The liquid preparations are suitable for use in cases of enlarged tonsils; after persevering treatment, improvement in nasal breathing can be observed, due to reduction of the swellings. Ulcers and fissures of the tongue have been painted with a solution of papain 1 to 2 in 10 each of glycerin and water.

Juice from the unripe fruit is very acid and acts as an efficient vermifuge, and is also a galactagogue and antiscorbutic.—S. G. Willmott, *Pharm. J.*, ii/1928, 219.

**Elixir Papaini (B.P.C.).**

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Contains 3 gr. of papain per drachm.

**Glycerinum Papaini (B.P.C.).**

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Papain 9% w/v in dilute hydrochloric acid, simple elixir and glycerin.

Is given with meals as a digestive; it has also been used as a pigment for chronic eczema and warts, and has been applied to diphtheritic exudation.

**Liquor Papaini et Iridini (B.P.C.).**

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Contains 1 gr. of pepsin and 1 gr. of extract of iris per drachm.

[P1-S1] **Pilula Papaini Composita.** *Dose.*—1 with meals.

Papain 2 gr., extracts of nux vomica  $\frac{1}{2}$  gr., belladonna  $\frac{1}{2}$  gr., aloes  $\frac{1}{2}$  gr. A digestive laxative.

[P1] **Syrupus Papaini (Fr. Cx.).** Papain 0.4, cherry-laurel water 0.4, alcohol (60%) 4.2, simple syrup 95, all by weight.

## PARAFFINUM

**Paraffinum Durum (B.P.).** *Syn.* PARAFFIN WAX, PARAFFINUM (U.S.P. XI, *Fr. Cx.*), PARAFFINUM SOLIDUM (P. Dan.). (PARAFFINUM SOLIDUM (P. Helv. V) is ceresin.)

A mixture of several of the harder members of the paraffin series of hydrocarbons from  $C_{21}H_{44}$  to  $C_{30}H_{62}$ ; obtained by distilling shale, separating the liquid oils by refrigeration and purifying the solid product. Colourless, semi-transparent, crystalline, inodorous and tasteless, slightly greasy to the touch. Sp. gr. 0.82 to 0.94. It burns with a bright flame, leaving no residue. Hard paraffins are supplied with various melting-points. B.P. specifies 50° to 60°; U.S.P. XI 50° to 57°.

**Soluble** about 1 in 80 of ether, slightly soluble in dehydrated alcohol, insoluble in water; also insoluble in acetone—a fact of value in the analysis of mixtures.

**Uses.** Principally as an ingredient of ointment bases, especially for protective ointments. Melted paraffin has been employed for the treatment of inflamed joints, sprains, etc. Injections of melted paraffin have been used in plastic surgery.

**Solid Paraffin Injections.** For subcutaneous injection in plastic operations this should be hard paraffin with m.p. 110 to 115°F., not an extempore mixture. Used to improve the size and shape of the nose, ear, etc., where abnormal, also for injecting into cavities after previously swabbing out with antiseptic lotion. The injection should be made in a warm room to allow of the flow of the melted substance through the syringe needle.

**Paraffinoma.** Two cases following paraffin injections. One of the rectum due to liquefied hard paraffin, the other stated to be due to an injection of camphor in liquid paraffin oil in the thigh.—A. T. Bazin, *Brit. med. J.*, ii/1929, 1102.

The publication of various cases of paraffinoma by authors in Europe and America has acted as a warning of the possible dangers of injecting mineral oil into the body tissues. A case of paraffinoma described.—Mason Bolam, *Brit. J. Dermat.*, 1935, 523.

**PAINFUL RHEUMATIC JOINTS.** Envelop the limb (previously shaved) quickly in a thin layer of melted paraffin at a temperature of 80° to 85° and add until layer is 1 to 2 cm. thick. Apply flannel bandage and leave on for 5 hours.—*per Practitioner*, i/1928, 397.

Paraffin wax bath over the whole body applied in sections at a time for applying heat to the skin.—H. W. Hales, *Lancet*, ii/1931, 586.

### Paraffin Treatment of Burns.

**Paraffin "No. 7"** is made as follows:—Melt hard paraffin 67.75 and add soft paraffin 25 and olive oil 5. Then mix in carefully betanaphthol 0.25 dissolved in eucalyptus oil 2, after the mixture has cooled to about 55°. (Resorcin 0.25 to 1% may be used as an alternative, with a small quantity of dehydrated alcohol as solvent.) The finished article melts at about 48°.

**Method of Use.** Wash the burns with sterile water, dry thoroughly, for example with a fan, and spray or apply the melted preparation carefully with a flat camel-hair brush. Cover with a thin layer of wool and a second coating. A preliminary application of 1 to 1000 acriflavine is useful.

**Paraffin "No. 7" Modified** has been made using spermaceti and hard paraffin *p. æq.*, instead of hard paraffin. The preparation

melts at 49° and is filled into rubber-capped tubes for use at time of operation, after melting in the water-bath.

**Ambrine** (*Anglo-French Drug Co., London*). A similar preparation advised by B. de Sandfort, containing a compound of paraffin with 5% of oil of amber. Applied in similar manner.

**Granulogen** (*Parke, Davis, London*). Chloretone 22 gr. per oz., and cresylic acid (0.5%) in a basis of paraffin, m.p. 46°. For the treatment of cutaneous lesions. To be melted and applied with a sterile brush or by means of a suitable spray.

**Paraseptic** (*Duncan, Flockhart, Edinburgh*). "Paraffin No. 7" composed of a mixture of paraffin wax eucalyptus oil olive oil and resorcin in the form of small cakes. When melted it acts as a first-aid dressing to burns, scalds, etc.

**Dental Wax.** Hard paraffin 1 oz., beeswax 6 oz., melt together, add  $\frac{1}{2}$  oz. alkanet and keep warm for 2 hours, then strain and add tincture of tolu 2 dr., otto of rose 5 drops. Generally supplied in sheet  $6\frac{1}{2}$  by  $3\frac{1}{2}$  inches.

**Use.** The sheet is warmed over the flame and moulded carefully over the model. It is used for mechanical purposes prior to vulcanisation.

**Ceresin.** A hard, white paraffin wax, m.p. about 65°, obtained by purifying ozokerite or earth wax, which occurs naturally near petroleum springs, especially in Galicia. Soluble 1 in 170 of ether, 1 in 125 of benzene and 1 in 80 of chloroform. Is used in the manufacture of candles and polishes.

**Paraffinum Liquidum** (*B.P., P. Helv. V, P. Dan.*). *Syn. and Prop. Names.* OLEUM PETROLEI, PETROLATUM LIQUIDUM (*U.S.P. XI*), CHRISMOL (*Allen & Hanburys, London*), COLONOL (*Kaylene, London*), DELECTOL (*Duncan, Flockhart, Edinburgh*), INTERNOL (*British Drug Houses, London*), NUJOL (*Stemco, London*), PAROLEINE (*Burroughs Wellcome, London*), PETREMOL (*Oppenheimer, London*), ETC.

**Dose.**— $\frac{1}{4}$  to 1 ounce (7.5 to 30 ml.).

A clear oily liquid obtained from petroleum after the more volatile portions have been removed by distillation. It consists of hydrocarbons ranging from  $C_{16}H_{34}$  to  $C_{21}H_{44}$ . Sp. gr. 0.880 to 0.895 (*B.P.*). For spraying, as also for "Toilet Paraffin," a less viscous oil is preferred with gravity 0.865 to 0.870, *vide* Paraffinum Liquidum Leve. For internal use a high gravity preferred. Below 0.880 it is not suitable as an internal lubricant. *B.P. Add. I* requires a kinematic viscosity of not less than 64 centistokes at 37.8°. *U.S.P. XI* has two varieties—one termed Heavy, the other Light Liquid Petroleum—with different viscosities.

Russian oil contains principally saturated hydrocarbons while American petroleum contains a large proportion of the unsaturated olefines. The Baku oils differ from Pennsylvania and other U.S. oils in consisting largely of hydrocarbons of the naphthene group (saturated single link ring compounds). American oils are best for chlorinating. *Cf. p. 396.*

**Uses.** Given internally, liquid paraffin acts as a lubricant, and is widely employed as a mild aperient in chronic constipation, especially in the presence of hæmorrhoids. It has no food value and, indeed, recent work has shown that it interferes with the organism's ability to absorb carotene from ingested food (*see*



A. C. Curtis and R. S. Ballmer, *J. Amer. med. Ass.*, ii/1939, 1785; and *Lancet*, i/1939, 462; in view of this finding it is suggested that the common practice of prescribing liquid paraffin at meal-times should be abandoned.

Externally, liquid paraffin may be used as an emollient to the skin in irritant conditions, and to remove crusts, and liquid paraffin dressings are stated to give relief from pain during the eruptive stages of herpes zoster. It also makes a good catheter lubricant.

It is used as a basis for laryngeal and nasal spray solutions or pigments, but for these purposes the *B.P.* oil is too viscous, and Paraffinum Liquidum Leve (*vide infra*) is preferable. *Alkaloidal bases are, in general, only slightly soluble in liquid paraffin.* A little oleic acid added assists solution.

**Oleum Petrolei Flavum and Huiles Lourdes de Pétrole.** Heavy petroleum oils—products from American petroleum distilling between 280° and 400°, sp. gr. 0.880 to 0.905. Used as a vehicle for hypodermic injections. For the suspension of insoluble mercurial salts, such as calomel, salicylate, succinimide, benzoate and yellow oxide of mercury, 1, 5 or 10% mixtures being employed.

**Oleum Vaselini Fluidum, syn. HUILE DE VASELINE FLUIDE (Fr. Cx.),** is prepared from Caucasian petroleum by purifying the fractions between 335° and 440°. Sp. gr. about 0.875, *i.e.*, it approximates Paraffinum Liquidum in character. Employed in Huile Grise, *q.v.* *F.E. VIII, P. Ital. V and P. Belg. IV* are similar.

**Emulsio Ole. Vaselinis (Fr. Cx.).** Oil of Vaseline about 60% emulsified with agar and Irish moss in water.

**Creosoted Oil.** (Calot's formula). Liquid paraffin 70 g., sterilised by heating for ½ hour. Allow to cool and add in order: creosote 5 g., guaiacol 1 g., iodoform (sterile) 10 g., ether 30 g. Used as a wound dressing.

Injection of 10 ml. weekly of Calot's fluid with olive oil in place of liquid paraffin of distinct value following aspiration of cold abscesses and in treatment of white swellings of joints. **Calot's No. 2 Paste:**—Phenol camphor 3 g.; naphthol camphor 3 g., guaiacol 8 g., iodoform 10 g., lanolin 150 g., spermaceti 100 g., of value for injection in sinus formation in disease of hip, spine and knee. 10 ml. injected into sinus at temperature of 103°, repeated every fourth day for 10 occasions. Contraindicated in albuminuria and septic infections causing pyrexia.—R. Pollock, *Lancet*, i/1927, 225.

**OTORRHEA.** Calot's solution of value. Instil 5 to 10 drops into ear canal. To get fluid into Eustachian tube close opening of external canal by pressing tragus against canal wall and bringing alternate pressure to bear on it so as to cause pumping action on mixture, and continue until patient feels medicament in throat. Repeat nightly for a week. When secretion becomes thin discontinue and dry up with insufflations of boric acid powder.—I. Hamick, *J. Amer. med. Ass.*, ii/1929, 66. Success in 85% of cases.—J. C. Scal, *Med. J. Rec.*, 1933, 244.

**Emulsio Paraffini Liquidi Alkalina (B.P.C.).**

*Dose.*—1 to 4 drachms (4 to 16 ml.).

Mixture of magnesium hydroxide 1 part and emulsion of liquid paraffin with agar 3 parts.

**Emulsio Paraffini Liquidi Composita (B.P.C.).**

*Syn.* EMULSIO PARAFFINI CUM AGAR ET PHENOLPHTHALEINO.

*Dose.*—As above.

The formula is as above, incorporating also phenolphthalein 1½ gr. per ounce.

**Emulsio Paraffini Liquidi cum Agar (B.P.C.).**

*Dose.*—1 to 4 drachms (4 to 16 ml.), or more if requisite, morning and evening. Children 1 to 2 drachms. Contains 50% *v/v* of liquid paraffin and 0.75% *w/v* of agar.

**Emulsum Petrolati Liquidi (U.S.P. XI).** *Average dose.*—1 ounce (30 ml.). Liquid petrolatum 50% with acacia or agar, etc., syrup and alcohol, and 0.004% of vanillin.

**Emuls. Paraff. Liq. c. Phenolphthalein. et Agar (N.I.F.).** Agar 36 gr., liquid paraffin 4 oz., phenolphthalein 16 gr., glycerin 390 m., acacia 60 gr., tragacanth 20 gr., glycerin of boric acid 112 m., sodium benzoate 18 gr., vanillin  $\frac{1}{4}$  gr., double chloroform water to 8 oz.

**Emulso Paraffini Liquidum cum Hypophosphitibus (B.P.C.).**  
*Syn.* EMULSIO PETROLEI CUM HYPOPHOSPHITIBUS.

*Dose.*—1 to 4 drachms (4 to 16 ml.).

Liquid paraffin 50% *v/v* with 1 gr. each of sodium and calcium hypophosphites per drachm.

**Mistura Magnesii Hydroxidi et Paraffini Liquidum (B.P.C.).**

*Dose.*—1 to 4 drachms (4 to 16 ml.).

Liquid paraffin 30% *v/v* emulsified in mixture of magnesium hydroxide by means of acacia, or by using an homogenising machine, in which case no acacia is needed.

**Magnol (Duncan, Flockhart, Edinburgh).** A preparation containing in each fl. dr. magnesium hydroxide 4 gr. in liquid paraffin. *Dose.*—1 to 2 teaspoonfuls.

**Parogenum (B.P.C.).** *Syn.* VASOLIMENT, LIQUID PAROGEN.

Liquid paraffin 40% *v/v* with oleic acid, ammoniated alcohol and alcohol 90%.

**Cristolax (Wander, London).** A compound of 50% of liquid paraffin with 50% of malt extract in powder form.

**Olgar (Parke, Davis, London).** Emulsion of refined liquid paraffin and agar.

**Petrolagar (John Wyeth, London).** An emulsion of liquid paraffin 65%, with agar. Also available with phenolphthalein  $\frac{1}{4}$  gr. per oz., cascara sagrada (14.72% of a bitterless liquid extract), or alkaline (with magnesium hydroxide.)

**Paraffinum Liquidum Leve (B.P.C.).** *Syn. and Prop. Name.*

SPRAY PARAFFIN, PARAFFINUM LIQUIDUM PRO NEBULIS, PAROLEINE (for spraying) (Burroughs Wellcome, London).

A variety of liquid paraffin of lower gravity and lower viscosity than the oil for internal administration, and more suitable for the preparation of sprays and brilliants.

Evidence is gradually accumulating that the aspiration of oily substances may lead to well defined pulmonary changes, generally known as lipid cell pneumonia. This condition can be produced experimentally by the intratracheal administration of oil, large doses producing bronchiectasis. It is a macrophage response with phagocytosis of oil droplets and can be produced by any oil, though cod-liver oil and liquid paraffin produce the most severe reactions.—J. H. Paterson, *J. Path. Bact.*, 1938, 46, 151.

**Paraffinum Molle (B.P.).** *Syn. and Prop. Name.* PETROLATUM (U.S.P. XI) and PETROLATUM ALBUM (U.S.P. XI), PETROLEUM JELLY, VASELINA (F.E. VIII), VASELINUM (P. Ital. V, P. Belg. IV, P. Helv. V, Fr. Cx.), VASELINE (Chesebrough Manufacturing Co., London).

A white (Paraffinum Molle Album) or yellow (Paraffinum Molle Flavum) semi-solid mixture containing some of the softer or more fluid members of the paraffin series of hydrocarbons from  $C_{15}H_{32}$  to  $C_{20}H_{42}$ . M.p. of the white variety 40° to 46°, of the yellow variety 38° to 46° (U.S.P. XI requires 38° to 54°). Is usually obtained by purifying the less volatile portions of petroleum.

**Soluble** in alcohol slightly, freely in ether, chloroform, and other organic solvents, insoluble in water and in acetone. When melted, it mixes with oil, and many waxes, oleates and oleic acid.

Soft paraffin is not readily absorbed, but is emollient, protective and useful as an ointment base for surface action.

For the treatment of minor burns on the face or hands the Ministry of Health recommends (1941) for use in the Emergency Medical Services gauze or lint impregnated with sterile soft paraffin (*see Tulle Gras*)—tannic acid should not be used on these areas. Similar emergency treatment should also be employed for serious burns in other parts of the body requiring admission to hospital (prior to coagulation treatment).

**Fructolax** (*Savory & Moore, London*). *Dose*.—2 to 3 drachms at bedtime. A laxative containing about 80% soft hydrocarbon with fruit basis.

**Glegg's Mixture** consists of 3 parts liquid paraffin and 1 part of white soft paraffin, flavoured with rosettol (or with  $\frac{1}{4}$  gr. of menthol per oz.). Applied twice daily by a nasal pipette to the back of the nose for the prevention and treatment of the common cold.—E. P. Poulton, *Lancet*, 1/1932, 933. If the cold cannot be aborted entirely by this treatment, at least it develops into a relatively mild affair.—E. P. Poulton and F. A. Knott, *Practitioner*, 1/1936, 28.

**Confectio Paraffini** (*L.H.*). *Dose*.—1 to 2 drachms (4 to 8 g.).  
Yellow soft paraffin 16 oz., alkanet root 42 gr., oil of lemon 32 m., oil of bitter orange 32 m.

**Oculentum Simplex** (*B.P.C.*). A sterile mixture of wool fat and yellow soft paraffin used as a basis for eye ointments of the *B.P.* and *B.P.C.*

All ointments for the eye should be made with the official basis of wool fat 10, soft paraffin 90, in accordance with the directions of the *British Pharmacopoeia*, unless otherwise ordered. If the medicament is readily soluble in water it should be dissolved in the smallest quantity of sterilised water. This solution should then be incorporated in the melted sterilised basis, and the mixture triturated continuously until cold. If the medicament is not readily soluble in water it should be finely powdered, thoroughly levigated with a small quantity of the basis and finally incorporated with the remainder.

The ointment should be packed in a sterilised container and stored in a cool place. Small collapsible tubes with special tapering ends are very suitable containers, since there is a much smaller risk of contamination than when a pot is used. The tubes are best filled by inverting them in cold water and pouring in the ointment, previously softened by carefully heating after the manner used for moulding suppositories. Sterilised soft gelatin capsules are also used as containers. This latter method of packing has the advantage that sufficient ointment for one dose may be placed in each capsule.

When the medicament is in the form of an aqueous solution of an alkaloidal salt emulsified in the basis, the action is exerted much more rapidly and is more powerful than when it is in the form of an alkaloid in solution or suspension in the base, because of the greater ease with which solution in the lachrymal secretion is effected.

**Paranol** (*B.P.C.*). An emulsion of water in wool fat and soft paraffin.

**Unguentum Paraffini** (*B.P.*).

White beeswax 2, hard paraffin 8, yellow or white soft paraffin 90.

Unguentum Paraffini made with hard paraffin (m.p. 54° to 57°) 27, soft paraffin 70, beeswax 3, is suitable for use with the atmospheric temperature 15°. May be modified to meet the exigencies of climate and temperature.

The addition of 3% of beeswax makes the ointment more uniform. A hard paraffin with somewhat low melting point, e.g., 46° to 52°, is best. Melt together and set aside to crystallise (or allow to cool on the water bath) and then mill, rub down, or sieve again.

A small quantity of wool fat added to soft or liquid paraffins enables the production of a stable emulsion, *vide* Paranol.

**Unguentum Simplex (B.P.).**

Wool fat 5, hard paraffin 10, yellow or white soft paraffin 85.

**Unguentum (U.S.P. XI).** *Syn.* SIMPLE OINTMENT. Wool fat 5, white wax 5, white petrolatum 90. *P. Jap. V* has yellow beeswax 1, sesame oil 2, melted together and stirred till cool.

**Petroleum Benzine** is the fraction distilling below 150°, sp. gr. below 0.750. This is used for cleaning purposes. *Benzine means petroleum benzine.* Distinguish from benzene (benzol), the product obtained from coal tar, *q.v.* On fractionation it yields various products such as mineral naphtha or benzolin (boiling range 70° to 95°), ligroin or petroleum naphtha (boiling range 90° to 120°), and petrol.

**Petroleum Leve (B.P.C., P. Dan., P. Helv. V).** *Syn.* PETROLEUM SPIRIT, PETROLEUM ETHER.  $C_8H_{18}$  = 72.1 principally. At least 95% distils between 60° and 70°, and has sp. gr. of 0.620 to 0.700. *P. Helv. V* requires 90% to distil below 60°, sp. gr. 0.65 to 0.67.

**Benzinum Purificatum (U.S.P. XI), syn. PETROLEUM ETHER,** is purified petroleum benzine. It has sp. gr. 0.634 to 0.660, and distils entirely between 35° and 80°. **Petroleumum (P. Belg. IV)** has sp. gr. 0.64 to 0.67, boiling-range 50° to 75°. Higher fractions of petroleum are white spirit or turpentine substitute (boiling-range 140° to 220°), illuminating or solar oils (various boiling-ranges up to 300°) and heavy lubricating oils.

**Kerosene.** Distilled from petroleum and has a boiling range of 150° to 300° with sp. gr. about 0.800 to 0.811. Is used as an illuminating and fuel oil.

Kerosene poisoning in children—4 cases with 1 death.—J. P. Price, *J. Amer. med. Ass.*, ii/1932, 214.

**Tar Oil Compound.** Cottonseed oil 20, tar oil 5, kerosene 74, oil of lemon-grass 1. For head lice; rub onto the scalp and then wash the head with a solution of soft soap 2 lb., borax 4 oz., in water to 1 gallon.—Minist. Hlth Memo. No. 230 (*H.M.S.O.* 1940).

**Lefroy's Crude Mineral Oil Emulsion.** *Syn.* PETROLEUM INSECTICIDE.

Crude mineral oil (kerosene) 110, soft soap 50 (whale oil soap is specified) with about 10 of water to form a jelly. For use against lice, fleas, flies, etc., both destroying them, preventing their further attack and thereby acting as a prophylactic to many forms of infectious disease. It is used like ordinary soap for washing. If a little be allowed to dry into the clothes vermin will not approach. The same effect is secured by rubbing a little over the skin.

**Cera Alba (B.P., U.S.P. XI, P. Helv. V, Fr. Cx.)** is obtained by bleaching yellow wax, **Cera Flava (B.P., U.S.P. XI, P. Helv. V, Fr. Cx.)**, the secretion formed by *Apis mellifica* (Order, Hymenoptera) and used by the insect to form the cells of the honeycomb. Soluble in warm ether, in chloroform and in fixed and volatile oils; sparingly soluble in cold alcohol 90%. M.p. 62° to 64°.

**Ceratum (U.S.P. XI).** White wax 3, benzoated lard 7.

**Cera Aseptica (B.P.C.).** A sterile mixture of white beeswax and almond oil containing 1% of salicylic acid.

**Horsley's Wax.** An aseptic wax for surgeons' use. Yellow beeswax 7, phenol 1, olive oil 2. It is employed warm at a temperature such that its consistence is just sufficiently soft for easy manipulation. It is heated at temperature of boiling water 5 minutes and then poured into saline or mercuric chloride solution at 105°F., from which it is used during the operation.

As a plugging for the exposed cancellous bone in drainage for empyema in tuberculous children—free drainage effected.—Denis Browne, *Lancet*, ii/1930, 736.

**Oxyrocceum Plaster (P. Helv. V).** Yellow beeswax 35, colophony 25, elemi 10, ammoniacum 5, galbanum 5, myrrh 5, Venice turpentine 12, saffron 1, extract of rhatany 2.

**Carnauba Wax** is a hard yellowish or greenish wax exuded from the leaves of *Copernicia cerifera* (Palme), m.p. about 85°, sp. gr. about 0.995. Is used in polishes.

**Japan Wax** is a fat obtained from the berries of various species of *Rhus*. It is a pale yellowish wax, becoming white externally on keeping. M.p. about 55°, sp. gr. about 0.995. Is used in polishes.

**Cetaceum** (B.P.C., U.S.P. XI, *P. Helv. V.*, *P. Dan.*). *Syn.* SPERMACETI, BLANC DE BALEINE (*Fr. Cx.*).

*Dose.*—8 to 30 grains (0.5 to 2 g.).

Spermaceti is a white, unctuous crystalline substance (m.p. 42° to 50°), obtained from *Physeter macrocephalus* and other species of whale, e.g., *Hyperoodon rostratus*. Consists chiefly of cetyl palmitate,  $C_{16}H_{31} \cdot COOC_{16}H_{33} = 480.5$ .

**Soluble** 1 in  $1\frac{1}{4}$  of chloroform, about 1 in 7 of ether, 1 in 50 of hot alcohol, and in carbon disulphide and oils. A common ingredient of cold creams. A good addition to theobroma suppositories for hot climates. An emulsion (with acacia or egg yoke, using spermaceti powdered with a little alcohol) has been administered as a demulcent for coughs.

**Oleum Cetacei** is obtained by removing the spermaceti which separates from the crude oil on standing. It is a thin yellow oil used for burning and as a lubricant.

**Unguentum Cetacei** (B.P.C.) contains 20% of spermaceti in white beeswax and liquid paraffin.

### Higher Fatty Alcohols.

The higher fatty alcohols are the higher members of the monohydric alcohol series. They occur in waxes or in the wax-like unsaponifiable constituents of some fats. As these sources with few exceptions are severely limited, the higher fatty alcohols are prepared by the hydrogenation of the higher fatty acids. Cetyl alcohol, however, is usually obtained from spermaceti. These alcohols are solid, white, crystalline substances, melting without decomposition. They are not acted upon by dilute alkalis or acids, and on boiling with alcoholic potash and diluting with water, they are precipitated unchanged. The alcohols dissolve in concentrated sulphuric acid in the cold to form alkyl sulphates, the sodium salts of which are known commercially as the sulphonated fatty alcohols. Two members of the higher fatty alcohols are important from the point of view of their use in cosmetic and pharmaceutical products, namely, cetyl and stearyl alcohols. They possess good emollient properties without being greasy, and added to water-in-oil emulsions, increase the viscosity, improve the texture, and aid the stability of the preparation. Moreover, the pure substances do not turn rancid. They possess emulsifying powers which allow the reduction, in formulæ for water-in-oil emulsions, of the other emulsifying agents used, and they are also readily absorbed by the skin, thus increasing the efficiency of the preparations containing them.

**Cetyl Alcohol.** *Syn.* ALCOHOL CETYLICUS (*P. Helv. V.*), ETHAL.  $C_{16}H_{33}OH = 242.3$ .

It occurs in spermaceti combined with palmitic acid. A white, tasteless, odourless, crystalline substance, greasy to the touch.

Cetyl alcohol is non-irritating, does not become rancid, and is stable to light and air. M.p.  $48^{\circ}$  to  $50^{\circ}$ ; b.p.  $344^{\circ}$ .

**Insoluble** in water; soluble in alcohol, chloroform, ether and other organic solvents. It is miscible with fats and oils.

Cetyl alcohol is of increasing importance in pharmacy and cosmetics. It forms water-absorbing emulsions, facilitating the inclusion of numerous medicaments, is readily included in compounded ointments, and is claimed to aid in the passage of certain medicaments through the skin. Cetyl alcohol is added in about 2 to 7% concentration to ointment bases, and in lesser proportion to stabilise emulsions. Equal parts of a 2% solution of cetyl alcohol in mineral oil, and a 1% soap solution, form a thick, stable emulsion. The alcohol has been found helpful in cream for eczema and pruritus. A common powder for such cases consists of equal parts of cetyl alcohol and boric acid. The preparation of ointments is described.—H. Goodman and A. Suess, per *Brit. chem. Abstr. (B)*, 1939, 1443.

**Unguentum Cetyllicum** (*P. Helv. V*). Cetyl alcohol 4, wool fat 10, white soft paraffin 86. This ointment is stated to exude water on standing, and may be improved by substituting stearyl alcohol for cetyl alcohol.

**Stearyl Alcohol.** *Syn.* OCTODECYL ALCOHOL.  $C_{18}H_{37}OH = 270.5$ .

Stearyl alcohol is obtained by the hydrogenation of stearic acid, and contains cetyl alcohol. It is a whitish, wax-like substance, neutral in reaction, and crystallises in large silvery laminae. M.p.  $59^{\circ}$ .

**Lanette Wax SX** (*Ronsheim & Moore, London*), consists of a partially phosphated (about 10%) cetyl-stearyl alcohol. It is a whitish, wax-like neutral substance, melting at about  $50^{\circ}$ , and easily self-emulsifiable to the oil-in-water type of emulsion. It is used as an emulsifying agent in cosmetics, ointments, hair-creams and other toilet preparations.

A new ointment base may be prepared as follows: Lanette Wax SX 15%, white soft paraffin B.P. 15%, water to 100%. The wax is shredded and melted and the white paraffin added. This is transferred to a warm jar and the water, previously heated, added with slow stirring. On cooling, with stirring, a base of fairly even texture is produced, which can, however, be greatly improved by homogenising while still warm and soft. The cost of the base is approximately that of B.P. lard. The base is of very wide application, acts as a detergent and is cosmetically elegant. It is not liable to rancidity, is non-greasy, and has excellent spreading qualities. It is neutral in action and does not exclude the cooling and heating action of air, and, if necessary, of light and sun. The skin surfaces can in most cases be readily visible even with this ointment on, as only a smear is required.—F. A. E. Silcock and A. Chamings, *Brit. med. J.*, ii/1939, 691.

**Halden's Emulsifying Base** (*J. Halden, Manchester*). *Syn.* "H.E.B." SIMPLEX.

Liquid paraffin 3, soft white paraffin 2, a mixture of higher fatty alcohols (hexadecyl and octadecyl alcohols) containing 10% acid esters (phosphated) of the alcohols 2.

"H.E.B." Simplex possesses the advantages of being neutral, stable in the presence of acid, alkali, metals and salts, and yielding an emulsion with water or aqueous solutions (it is thus readily removed from the skin by water alone). Oil-soluble and water-soluble medicaments can be simultaneously conveyed to the skin, and it has been used as a base for ointments in the treatment of acne, rosacea and seborrhoea with encouraging results.—P. B. Mumford, *Brit. J. Derm. Syph.*, 1938, 50, 542.

## PELLETIERINA

[P1] "Alkaloids, the following; their salts, simple or complex:—Pomegranate, alkaloids of."

[S1] "Alkaloids, the following; their salts, simple or complex:—Pomegranate, alkaloids of, except substances containing less than 0.5% of the alkaloids of pomegranate."

[83] "*Alkaloids:—Pomegranate, alkaloids of—in pomegranate bark.*"

[86] "*Alkaloids:—Pomegranate, alkaloids of—specify proportion as the proportion of any one alkaloid of pomegranate that the preparation would be calculated to contain on the assumption that all the alkaloids of pomegranate in the preparation were that alkaloid.*"

*Dose.*—2 to 8 grains (0.12 to 0.5 g.).

A mixture of alkaloids obtained from pomegranate stem and root bark, *Punica Granatum* (Punicaceæ), the chief of which are pelletierine (punicine), a colourless liquid absorbing oxygen and becoming brown on exposure, and pseudo-pelletierine. Their amount varies between 0.5 and 0.9%. In addition the bark contains about 20% of tannin.

[P1-81] **Pelletierinæ Sulphas.** *Syn.* PUNICINE SULPHATE, PELLETIERINUM SULFURICUM (*Fr. Cx.*).  $(C_8H_{15}NO)_2 \cdot H_2SO_4 = 380.3$ .

*Dose.*—2 to 8 grains (0.12 to 0.5 g.).

Consists mainly of the sulphates of pelletierine and iso-pelletierine. Colourless crystals becoming yellow on keeping. It has been employed as a remedy for tapeworm, but is not so effective as the tannate.

The name pelletierine should be strictly reserved for the pure, optically active alkaloid so named by C. Tanret. Commercially, however, the name is applied to the total alkaloids of the stem and root bark of pelletierine. It is believed that the anthelmintic value of the bark depends chiefly on the content of *l*-pelletierine and its racemic isomer. From this point of view, the pelletierine sulphate of *Fr. Cx.*, which consists essentially of a mixture of the total alkaloids, from which the weak bases have been largely eliminated, appears to be more satisfactory therapeutically.—J. A. Goodson, *Quart. J. Pharm.*, 1940, 57.

[P1-81] **Pelletierinæ Tannas** (*B.P., U.S.P. XI*).

*Dose.*—2 to 8 grains (0.12 to 0.5 g.). *U.S.P. XI* average dose 4 grains.

A mixture of the tannates of the alkaloids. A light yellow powder. Soluble about 1 in 700 of water, and about 1 in 80 of alcohol 90%; insoluble in chloroform.

It has a specific action on tapeworms, but it is inadvisable to administer it to children owing to its toxic effects. For adults the dose is 5 to 8 grains, given in a little water on a fasting stomach, and followed in two hours by an ounce of castor oil.

**Granati Fructus Cortex** (*B.P.C.*). *Syn.* POMEGRANATE RIND.

*Dose.*— $\frac{1}{2}$  to  $\frac{1}{4}$  drachm (1 to 2 g.).

The dried pericarp of the fruit of *Punica Granatum* (Punicaceæ). It is a powerful astringent and is used as a decoction in diarrhoea and as a douche in leucorrhœa. Contains about 28% of gallotannic acid.

**Granati Radicis Cortex** (*B.P.C., P. Helv. V, P. Dan.*). *Syn.* GRANATI CORTEX, GRENADIER (*Fr. Cx.*), POMEGRANATE, MELOGRANO (*P. Helv. V*).

*Dose.*— $\frac{1}{2}$  to  $\frac{1}{4}$  drachm (1 to 2 g.).

The dried bark of the stem and root, containing about 0.5 to 0.9% of alkaloids, chiefly pelletierine and pseudo-pelletierine. Used to expel tapeworm, the 1 in 5 decoction being given in doses of 2 ounces every two hours for four doses, the treatment being preceded and followed by the administration of a purge.

Better results have been claimed in tapeworm by passing into the duodenum by Einhorn's catheter 150 g. of powdered root bark infused for 12 hours in a litre of water, and boiled down to one half. Before use, warm to 100°F. and give three doses of 65 ml. at half-hour intervals, followed by laxative, after which catheter is withdrawn.

**Spigelia.** *Syn.* INDIAN PINK, PINK ROOT. *Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 g.). The dried rhizome and rootlets or the dried entire plant, *Spigelia marilandica* (Loganiaceæ). Anthelmintic for round-worms, being administered in conjunction with a purge either as powder or as an infusion. Should be followed by a saline purge.

## PEPSINUM

*B.P., U.S.P. XI, Fr. Cx., P. Helv. V.*

*Dose.*—5 to 10 grains (0.3 to 0.6 g.) either with or immediately before or after meals, in a pill or cachet. It is not unpalatable sprinkled on meat like pepper. *U.S.P. XI* average dose 8 grains.

A proteolytic enzyme obtained from the gastric mucous membrane of the pig, sheep or calf, *Pepsina Porci* being usually preferred. Occurs as a light, yellowish-brown powder or in translucent scales or granules. It is supplied to dissolve 2500 (*B.P.*), 3000, 5000, or up to 10,000 times its weight of freshly coagulated egg albumen. *U.S.P. XI* requires it to digest 3000-3500 times its weight of egg albumen. Pepsin may be adjusted to a required strength by the addition of lactose.

**Incompatibility.** Its activity is destroyed by more than traces of salt, by boiling its solution, by heating in the presence of alkali, and by pancreatic ferments in neutral solution. It is active in the presence of dilute acid, but its activity is destroyed by more than about 0.5% of hydrogen chloride.

**Uses.** As a digestive, small doses, either in the form of powder, cachets or one of the following preparations. Pepsin and hydrochloric acid given immediately after eating may inhibit carbohydrate digestion in the stomach. It should not be taken until 30 to 45 minutes after a meal. It may be found of value in combination with hydrochloric acid in advanced achlorhydric (microcytic) anæmia and in Addison's anæmia, and it is claimed to have given good results in sprue and hill diarrhœa. Pepsin is also administered in tablet form with or without other ingredients, and in mixture form with bismuth. For the composition of a useful acid mixture containing bismuth sodium tartrate, *see* p. 304.

**GASTRIC AND DUODENAL ULCERS** (600 cases) cured by subcutaneous injections of a 1% pepsin solution (freed from albumin by pressure filtering through clay and containing phenol). Begin with 0.2 ml. thrice daily or every other day, increasing by 0.1 ml. to 0.5 ml., repeating this for 12 injections, and then decreasing in the same way to 0.2 ml. Injections said to be harmless and painless. Give olive oil before meals and bismuth after meals. Avoid belladonna and sodium bicarbonate, and give mixed diet.—K. Glaessner (Vienna), *Lancet*, i/1932, 78.

Achlorhydria in a variety of conditions cured by pepsin and hydrochloric acid.—T. H. Oliver and J. F. Wilkinson, *Brit. med. J.*, ii/1930, 1048.

**Elixir Pepsini** (*B.P.C.*).

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Contains about 3 gr. of pepsin per drachm.



**Glycerinum Pepsini (B.P.C.).**

*Dose.*—1 to 2 drachms (4 to 8 ml.) in water.

A solution of pepsin 10% *w/v* in acidified glycerin and water. This is a very active solution. If made with good scale pepsin it keeps indefinitely.

**Mist. Acid. Pepsin. (N.I.F.).** Dilute hydrochloric acid 10 m., glycerin of pepsin 30 m., water to  $\frac{1}{2}$  oz.

**Glycerinum Pepsini Fortius (B.P.C.).** *Syn.* GLYCEROL OF PEPSIN.

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Contains about 8 gr. of pepsin per drachm, in acidified glycerin, simple elixir and water.

**Liquor Pepticus (B.P.C.).**

*Dose.*—1 to 2 drachms (4 to 8 ml.).

Contains 1 in 8 of stronger glycerin of pepsin in acidified diluted alcohol.

[P1] **Liquor Diastos (Sharp & Dohme, London).** A compound pepsin preparation containing in each fluid ounce: pepsin (1 in 3000) 8 gr., papain  $1\frac{1}{2}$  gr., rennin  $\frac{1}{2}$  gr., dilute nitrohydrochloric acid 5 m., lactic acid  $\frac{1}{2}$  m., nux vomica  $\frac{1}{2}$  gr. *Dose.*—A dessert to a tablespoonful, before or after meals, as indicated. Achylia gastrica, atonic dyspepsia, and faulty digestion.

**Liquor Pepticus (Benger) (Benger's Food Ltd., Manchester).**

*Dose.*—1 to 2 drachms (4 to 8 ml.) in a wineglassful of water with meals. An active solution of the ferments in weak alcohol.

**Pulvis Pepsini Compositus (B.P.C.).**

*Dose.*—10 to 30 grains (0.6 to 2 g.).

Pepsin 15%, pancreatin 10%, diastase 1%, with lactic and hydrochloric acids and lactose.

**Peptana (Burroughs Wellcome, London).** Tablets contain pepsin, pancreatin and calcium lactophosphate, of each 1 gr. The external sugar-coating dissolves in the stomach, exposing the pepsin, whilst the pancreatin enclosed in a keratin coating dissolves in the intestine.

**Vinum Pepsini (B.P.C.).** *Dose.*—1 to 2 drachms (4 to 8 ml.) with meals.

Contains pepsin 2 gr. per drachm, hydrochloric acid 1 in 80 and glycerin in sherry-type wine.

**Peptenzyme (Reed & Carmick, Jersey City; Coates & Cooper, London).**

*Dose.*—10 to 20 grains (0.6 to 1.2 g.) before or after meals and at bedtime. A preparation containing the enzymes which enter into the process of digestion. Suitable for varied types of indigestion. Also supplied in tablets, granules and elixir.

**Seriparium (B.P.C.).** *Syn.* RENNET, RENNIN.

The partially purified, milk-curdling enzyme from the glandular layer of the fourth or true digesting stomach of the calf, occurring as greyish- or yellowish-white scales or powder slowly soluble in water. It deteriorates when stored. Coagulates not less than 25,000 times its weight of fresh cows' milk.

**PEPTONUM**

*B.P.C.*

*Dose.*—5 to 15 grains (0.3 to 1 g.);  $\frac{1}{8}$  to  $1\frac{1}{2}$  grains (0.01 to 0.1 g.) by injection.

A mixture of cleavage products of proteins consisting of proteoses with peptones and amino-acids, prepared from meat and other proteins by enzymatic degradation or other processes. It occurs as a whitish or buff-coloured powder, usually soluble in water. It varies much in composition according to the method of preparation and the purpose for which it is required. Peptone is used for making solutions for injection and as a constituent of culture media in bacteriology.

**Injectio Peptoni (B.P.C.).**

*Dose.*—3 minims (0.2 ml.) gradually increased to 25 minims (1.5 ml.) by intravenous or intramuscular injection.

A sterile neutral solution containing 5% *w/v* (for intravenous use), or 7.5% *w/v* (for intramuscular use) of peptone (*vide infra*).

**Non-Specific Protein Therapy**

Non-specific protein therapy is the treatment of disease by the injection of proteins, either bacterial or non-bacterial, which, by provoking a defensive reaction (rise of temperature, leucocytosis, etc.) similar to that produced by the invasion of the organism by a specific foreign protein, enables the patient to desensitise or immunise himself. The actual mechanism of this reaction is still obscure.

Numerous substances have been employed to produce this protein shock. Amongst the more important of these are (1) peptones; (2) milk and preparations made from milk; (3) vaccines (used non-specifically) and tuberculins; (4) artificially induced diseases, such as malaria; (5) blood; (6) vegetable and animal proteins, such as pollen extracts. These are dealt with in this order in the following pages.

(1) **Peptone Injections.** Peptone injections are employed for non-specific desensitisation in allergic conditions, particularly in asthma, hay fever, angioneurotic oedema, urticaria and cyclic vomiting. The injections may be given either intravenously or intramuscularly. For *intravenous treatment* in asthma a 5% solution is employed, and this is given in a series of ten graded doses, commencing with 0.3 ml. and gradually increasing up to 1.5 ml.; this is followed by a further course of six injections (three of 2 ml. and three of 2.5 ml.) given every fourth or fifth day. For *intramuscular treatment* a similar course of injections is given, employing a 7½% solution.

Though this form of non-specific desensitisation often gives extremely good results in asthma, certain types of cases are completely resistant; these include many of those with chronic bronchitis and developed emphysema, and cases presenting any degree of cyanosis, also those in whom, apart from asthmatical paroxysms, a more or less oppressed condition of the respiration is practically never absent. Children frequently respond well to the treatment, especially where the asthmatic attacks are of the clear-cut spasmodic type, but a small initial dose should be given to test the sensitivity of the patient.

(The treatment outlined above refers to the use of Armour's Peptone No. 2. A more potent preparation, known as Witte's peptone, or "Peptone Witte Special 30" and containing a higher proportion of primary proteoses, has also been employed in non-specific protein therapy, but in much lower dosage, e.g., 0.2 ml. of a 1% solution intramuscularly, gradually increased by 0.2 ml. at weekly intervals to 1.2 ml. It has also been employed orally in various allergic conditions, in a dose of 8 grains three times daily, before meals.)

**ASTHMA.** Treatment by desensitisation, though still empirical, has given very good results in some cases.—*Lancet*, ii/1931, 1140.

It is an undeniable fact that a small injection of animal protein in high dilution has very marked effect on the spasmodic attack associated with asthma.—T. Nelson and A. D. Porter, *Lancet*, ii/1931, 1344.

Asthma due to protein sensitiveness (dog). Opinion divided as to peptone.—C. J. Murphy, *Lancet*, i/1931, 813. Asthma well treated.—J. Mowbray, *Lancet*, i/1931, 813.

**Eupepton** (Allen & Hanburys, London). Therapeutic and bacteriological peptones. No. 1. For injection in non-specific protein therapy and for preparation of the culture medium for the Rideal-Walker test. No. 2. For preparation of culture media for general bacteriological purposes.

**Paragen** (Bayer Products, London). Described as a polypeptide and quino-line-urea compound with protein degradation products for intramuscular injection in the non-specific treatment of infective arthritis and other infections. Dose.—2 ml. once or twice daily.

(2) **Milk Injections.** Injections of sterilised milk (or milk proteins) have been employed as a form of protein shock therapy, the dose usually given being from 5 to 10 ml. intramuscularly. The injections give rise to a generalised anaphylactic reaction, characterised by chill, malaise, and a rise in temperature, and good results have been claimed for the treatment in acute gonorrhœa, erysipelas, and general paralysis of the insane.

**ERYSIPELAS.** Rapid recovery in 15 cases following intragluteal injection of 5 ml. Contraindications: pulmonary tuberculosis and chronic recurrent hematemesis.—*Brit. med. J. Epit.*, i/1928, 85.

An injection of 10 ml. of boiled milk intramuscularly promotes a cure within 12 hours.—*Brit. med. J.*, i/1938, 764.

**LEPROSY** well treated by intravenous milk injections. 12 cases treated with sufficiently good results to enable them to resume their employment. The treatment is drastic and dangerous and especially applicable to the late and more hopeless forms of the disease.—N. A. Dyce Sharp, *Trans. R. Soc. trop. Med. Hyg.*, Jan., 1928, 308.

**Aolan** (Herts Pharmaceuticals, Welwyn Garden City). Milk protein preparation for intramuscular injection in non-specific therapy.

(3) **Non-specific Vaccines.** Various vaccines have been employed including *B. coli*, gonococcus, streptococcus and typhoid, of which the last-mentioned is the most popular. T.A.B. vaccine has been injected intravenously with some measures of success in rheumatoid arthritis, chorea, G.P.I. and various forms of vascular disease. It is diluted with physiologic solution of sodium chloride until 1 ml. contains 100 million organisms; the initial dose for adults is from 10 to 25 million. Tuberculin has also been used, particularly in the treatment of asthma.

**ARTHRITIS.** T.A.B. vaccine intravenously produces rapid improvement in 80 to 90% of cases, which is maintained in between 50 and 60%, the types responding best being acute and subacute, where disease is confined to the peri-

articular tissues. Injections of no use unless all possible foci of infection removed. Reactions severe, but contraindications few—disease of myocardium, gross kidney disease, chronic alcoholism, tuberculosis and syphilis being the chief. Cases of the menopause group, of the chronic villous type and those showing achylia do not do well. Initial dose 100 million (in private practice 50 million), increased at each subsequent dose by 100 million, 4 days elapsing between injections. Dosage should be regulated to produce rigor, sharp rise of temperature, quick fall, and profuse perspiration. Of 50 cases treated 44 were discharged after 4 weeks as definitely improved.—W. Yeoman, *Lancet*, i/1926, 1246-50; see also *ibid.*, 1265.

**ASTHMA.** True cases of bronchial asthma benefited by prolonged injections of P.T.O. dilutions, beginning with 0.5 ml. of 1 in 1,000,000 and gradually increasing. The treatment must be kept up for a year at least and injections twice a week are given for the first 4 months, then once a week for 4 months, and lastly once a fortnight.—T. Nelson, *Practitioner*, i/1927, 382.

**CHOREA.** Treatment by pyrexia induced by intravenous injection of triple typhoid vaccine containing 1000 million typhoid and 750 million each of paratyphoid A and B per ml., beginning with 0.05 or 0.1 ml., the object being to attain a temperature of 104° to 105.5° and to maintain it for four hours. Treatment continued daily till choreic movements have disappeared—usually within a week.—D. Bateman, *Brit. med. J.*, i/1933, 1003. See also J. W. Cheetham, *ibid.*, 1130.

**GENERAL PARALYSIS.** Typhoid vaccine as a substitute for malaria therapy, *q.v.* T.A.B. containing 100 million *B. typhosus* and 750 million *B. paratyphosus* A and B, intravenously, 1 ml. for 10 days, starting with 300 million total, and rising to 6000; then 6 weeks' interval and recommence with 1500 million, rising to 20,000 in 10 days, with 4 injections of neoarsphenamine in the interval. Remission induced. Contraindications—arteriosclerosis, pulmonary disease, myocardial and advanced cardiovascular disease, and marked focal infections.—J. M. Mackenzie, *per Prescriber*, 1929, 302; *Lancet*, i/1929, 288.

**SCIATICA** of the sacro-iliac joint: T.A.B. vaccine intravenously gives the best chance of removal of symptoms in the shortest possible time.—W. Yeoman, *Lancet*, ii/1928, 1119.

**VASCULAR DISEASE.** One of the newer fields for foreign protein therapy is that of vascular disease, particularly thrombo-angiitis obliterans, the pain of which is often excruciating, and Brown considers the intravenous administration of typhoid vaccine the best medical measure for its relief. Allen and Smithwick have reported successful results with typhoid vaccine in Buerger's disease, in the gangrene of arteriosclerosis, and in purely vasomotor types of vascular occlusion. These authors used doses of from 125 to 300 million bacilli but Wright believes that the chill should be avoided and recommends small doses just enough to produce 2 or 3 degrees of fever. Wright recommends an initial dose of 10 million typhoid bacilli, with an increase of 10 million with each subsequent injection. Goodman and Gottesman have also reported enthusiastically on the use of fever therapy in vascular disease, particularly Raynaud's disease.—R. L. Cecil, *J. Amer. med. Ass.*, ii/1935, 1852.

**Omnadin** (*Bayer Products, London*). Compound sarcine vaccine containing albumins, lipoids and fats. *Dose*.—2 ml. intramuscularly daily. Non-specific therapy in all fevers and in acne and furunculosis.

**(4) Artificially Induced Disease.** This procedure is based on the principle that remissions in chronic disease may occur after an attack of acute specific fever, and it has been especially employed in the treatment of G.P.I. by the artificial induction of malaria. Subcutaneous injections are given of from 2 to 4 ml. of blood from the vein of a patient suffering from benign tertian malaria. After an incubation period of from 10 to 20 days, the temperature rises and the patient has a rigor. From nine to twelve paroxysms are allowed and the infection is then terminated by quinine. The mode of action of the malaria is uncertain, but the hyperpyrexia produced is probably the most important factor.

In treatment of general paralysis a rigor on alternate days is followed by greater benefit than a daily rigor. Allow the primary attack to go on 4 or 5 days then give 3 to 5 gr. of quinine to check temporarily and wait for relapse. In this way the temperature is nearly always of the true tertian character with rigors on alternate days.—Leader, On Report of First Results of Laboratory Work on Malaria in England.—Col. S. P. James and P. G. Shute, *Brit. med. J.*, ii/1926, 79.

Watch should be kept for undue enlargement of spleen, especially if patient has previously had malaria.—N. G. Harris, *Lancet*, ii/1928, 500.

Allow at least 8 rigors. Malaria effectively cured by quinine. No relapses with inoculated malaria—compared with 50% relapses with mosquito bites. Follow up with 3 g. of tryparsamide intravenously and 0.2 to 0.4 g. of bismuth intramuscularly weekly in 10-week courses with intervals of 4 weeks.—R. Lees, *Brit. med. J.*, ii/1931, 338.

Ten years of malaria therapy: results in 368 cases. It undoubtedly improves the bodily health, prolongs life to a marked degree in some 35% of cases, and has beneficial action on habits and cleanliness. In 18 to 20% it produces clinical improvement apparently lasting many years, and often allows resumption of healthy and useful home life.—J. E. Nicole and E. J. Fitzgerald, *Brit. med. J.*, i/1934, 427.

**(5) Whole Blood Injections.** A simple and effective form of non-specific desensitisation is injection of the patient's own blood (autohæmotherapy). From 5 to 10 ml. of blood is withdrawn and immediately re-injected intramuscularly. These injections have been employed in a wide variety of conditions, and in particular have often been found of value in chronic dermatoses, including eczema, pruritus, psoriasis, pemphigus, and urticaria.

Of all the methods of desensitisation by non-specific injections, whole-blood therapy has much to recommend it. When indicated it should always be used first before recourse is had to more elaborate procedure.—C. Hardwick, *Practitioner*, i/1940, 79.

**ASTHMA.** Twenty-four asthmatic children received 5 injections each of 10 ml. of their own blood, which was withdrawn from the median basilic vein and injected immediately into the buttock, without admixture with citrate or separation of either plasma or serum. Observations over a period of 6 to 12 months afterwards indicated that in approximately three-quarters the frequency of attack was appreciably reduced and in every instance some alleviation of severity was manifest.—K. Maddox and R. F. Back, *Arch. Dis. Childh.*, 1935, 380.

**TYPHUS.** 16 severe cases treated by intramuscular injection of 10 ml. of the patient's blood. Each injection was followed by an immediate improvement in the general condition, and the duration of the disease seemed to be shortened by a series of 4 or 5 injections.—A. Babalian, per *Med. Annu.*, 1935, 463.

**WHOOPIING-COUGH.** After failure of vaccine therapy 20 severe cases in children aged from 25 days to 30 months in the paroxysmal stage were treated by one or two intragluteal injections of maternal blood; all but three showed rapid improvement.—V. de Gironcoli, per *Med. Annu.*, 1936, 509.

**Antibacsyn (Antibody Products, Watford).** A preparation derived from ox serum, "consisting of a suspension in carbol saline of serum euglobulin adsorbed to the hydroxides of calcium and magnesium." For use wherever protein therapy has been found effective. *Dose.*—1 or 2 ml. subcutaneously.

**Edwenil (Endocrines-Spicer, Watford).** Described as a deproteinised flocculus obtained by fractionation from an extract of beef muscle and normal horse serum suspended in 0.5% phenolised normal saline. It is stated to arouse the defences by stimulation of the reticulo-endothelial system and other defence mechanisms, and to produce rapid response in endotoxic infections without causing undesirable reactions. Advocated in pneumonia and diseases of the respiratory tract, also in furunculosis and whooping cough. *Dose.*—2 to 4 ml. subcutaneously every 12 hours in acute infections, 2 ml. daily in less acute conditions, and 2 ml. on alternate days in chronic infections. Contraindicated in acute infective processes where there is no drainage, e.g., acute appendicitis, sinusitis, cholecystitis and mastoiditis.

(6) **Vegetable and Animal Proteins.** Hay fever and most forms of asthma are due to a peculiar reaction of the tissues ("anaphylaxis") of sensitive individuals to certain proteins which are inhaled in the air or swallowed with food. Some individuals are sensitive to only one protein and others to a large number. The proteins to which sensitisation is most frequent are (1) pollen proteins, (2) epidermal proteins (from animal hair or feathers), (3) food proteins, and (4) bacterial proteins. It is frequently possible to determine by a cutaneous or, especially in the case of pollen sensitisation, by an ophthalmic reaction, employing test solutions of protein extracts, whether a patient is susceptible to a particular protein or group of proteins. In the skin test the protein extract is introduced either intradermally, by scarification, or by merely pricking the skin, using on an adjacent spot a control of normal saline, the areas usually chosen for the test being the forearm in men and the front of the thigh in women and children. In the case of a positive reaction a wheal will begin to appear within 5 minutes. The ophthalmic reaction consists in a slight reddening of the eye within 5 minutes of the instillation of a solution of a pollen extract into the conjunctival sac. The normal man never gives this reaction. The offending protein having been discovered the patient is then given a course of injections with the appropriate desensitising agent.

In England, the true hay fever due to grass pollen is a hundred times more important than all the other pollen fevers together. Extracts from all the various grass pollens furnish one and the same antigen for purposes of desensitisation to hay fever.—J. Freeman, *Lancet*, i/1933, 573.

From an allergic study of 262 cases of dermatoses, including eczema, urticaria, prurigo, dermatitis venenata, etc., it was concluded that intradermal tests were of little value in determining the cause; though positive reactions were frequently obtained they were rarely of practical significance. The indiscriminate subjection of patients with dermatoses to a large number of skin tests is not justifiable.—H. V. Mendelsohn, *Arch. Derm. Syph.*, N.Y., 1934, 845.

Over 90% of 961 patients treated for hay fever in 1932 and 1933 were cured or relieved by prophylactic subcutaneous injections of pollen antigens. A mixed standard preparation containing extracts of all pollens found to be pathogenic in Central Europe preferable to searching for some specific antigen.—K. Hansen, per *Lancet*, ii/1935, 201.

The various regions of the body do not react alike to skin tests. The back reacts more strongly than the upper arm, the flexor surfaces than the extensor, the upper arm than the forearm. Hence in comparing results one must make sure that all tests were made on the same region of the body. For instance, one should not compare a test made on the back with one made on the forearm. As to the back itself, wheals induced four fingerbreadths below the spine of the scapula were only half as large as those produced in the region of the spine of the scapula itself.—W. Schmidt, *Klin. Wschr.*, 1935, 14, 378.

In choosing which skin tests to apply, it is well to remember that after infancy such inhalants as feathers, dusts, animal emanations and pollen, play a much greater part than foods, and treatment with such substances is more likely to be successful than any dietetic measures. In a study of 300 children with asthma, positive scratch tests showed 47% sensitive to animal emanations, 29% to pollens, 25% to foods, and 5% miscellaneous.—G. W. Bray, *Practitioner*, ii/1937, 363.

The intranasal application of a pollen solution is invaluable in hay fever, both as a preventive of attacks and for use in relieving an existing attack. It is convenient to arrange that the desired dose is contained in 0.25 to 0.5 ml. of fluid, as this is a suitable amount to apply at one time. Necessary dilutions of concentrated pollen solutions may be made with 0.5% phenol in normal saline. For preventive purposes, before the hay fever season begins, commence with 100 to

200 units of pollen solution, followed by a 30% increase at intervals of two days or more. In an average case seen during the season, with mild symptoms, give an initial dose of 10 units and repeat in 5 minutes if this does not produce mild sneezing; subsequent doses may be increased 25% at intervals if necessary. The solution should be sprayed on to the septum, the middle and inferior turbinates, and on any hypersensitive areas.—C. Francis, *Brit. med. J.*, ii/1938, 1263.

E. R. Boland carried out investigations on the results of treatment by "desensitising injections" of proteins in the Asthma Research Clinic at Guy's Hospital. He found that the treatment had a beneficial effect in subduing the symptoms, but these effects were in no way superior to a control series in which equivalent volumes of normal saline solution were injected with similar ceremonial. In the treated cases and the control series the effects were equally transitory and were, in his opinion, psychological. It is not doubted that some cases of asthma are of allergic etiology, but it would seem that this is neither the most important nor the commonest factor.—G. Marshall, *Practitioner*, ii/1939, 489.

**Standardisation of Pollen Allergens.** As the exact nature of allergens is uncertain, there is no uniformity of standardisation. The following methods are used:— (1) Noon Unit—the quantity of extract obtained from 0.001 mg. of pollen. 1 Noon unit is equivalent to 80 to 100 pollen grains. (2) According to dilution (1 : 100; 1 : 1000; 1 : 10,000) of the weight of pollen per volume of menstruum. (3) According to amount of nitrogen found by precipitation of protein with phospho-tungstic acid, or trichloroacetic acid. (4) According to total nitrogen content.—J. J. Blackie, *Pharm. J.*, i/1938, 355.

**Numerous Allergenic Protein Preparations** have been accepted by the Council on Pharmacy and Chemistry of the A.M.A., and they are required to comply with the regulations of the U.S. Treasury Department regarding potency, sterility and labelling. They include allergenic extracts of numerous vegetable and animal substances, and concentrated pollen antigens, extracts, and solutions of a large number of plants.—N.N.R., 1940.

**Mixed Inhalants Solution (Bencard, London).** Proteins from feathers, animal hair, dust and orris root, with peptone. Also available without peptone. Adrenaline is also added to prevent a general reaction in sensitive patients. Available in two strengths, ordinary and continuation course. 10 ml. of the ordinary strength is usually sufficient for one patient.

**Pollacine (Parke, Davis, London).** A grass-pollen vaccine prepared from the pollen of Timothy grass and used for the prophylaxis and treatment of hay fever.

**Pollergen (Duncan, Flockhart, Edinburgh).** A combined pollen vaccine prepared in a series of 12 graded doses ranging from 50 to 15,000 Noon units for the treatment of hay fever.

**Peptonum Bovinum.** *Syn.* BEEF PEPTONE, DIETETIC PEPTONE. Is prepared by the action of pepsin on minced lean beef. Occurs as a white or yellowish powder or scales. Administered as lozenges (5 grains), enema (2 to 4 ounces of 1 in 8 solution), or as Suppositorium Nutriens.

Peptone may be manufactured by digesting 1 kilo of beef with 10 litres of water (containing 4 g. of hydrochloric acid per litre) with pepsin 10 g. for 8 hours at 50° with frequent shaking. Termination of reaction shown by absence of precipitate with nitric acid on adding to a little of the filtered liquid. Evaporate. 1 kilo yields 250 g. approximately.

**Suppositorium Nutriens (B.P.C.).** *Syn.* SUPPOSITORIUM PEPTONI. Contains 75% of beef peptone with gelatin and water.

**Carnrick's Liquid Peptonoids (G. W. Carnrick, New York; Brooks & Warburton, London).** A predigested food prepared from beef, milk and wheat, with wine. *Dose.*— $\frac{1}{2}$  tablespoonful at intervals.

**Panopepton (Fairchild Bros. & Foster, New York; Burroughs Wellcome, London).** A medicated wine prepared from beef and wheat.

Both the above may be dispensed by registered chemists without requiring a spirit licence to be taken out, providing it forms a constituent of a *bona-fide* medical prescription given by a duly qualified medical practitioner.

## MEAT EXTRACTS

**Meat Extract.** The meat is cut up and all tendons removed. It is then minced and boiled. After settling, the soup is skimmed to remove the fat. Next it is filtered and evaporated to 25 Beaumé, and it then contains 16% moisture. The whole process takes 5 days, and 10 lbs. meat gives 1 lb.

Meat extracts have a stimulant action on the gastric mucosa. The water-soluble fraction of meat is almost as efficient in stimulating a flow of HCl as whole meat. The secretion of HCl is greater with Bovril than with any other substance examined (gruel, beef powder, extracted beef, direct extract, Bovril, sodium glutamate), including whole meat. Whole meat in the form of beef powder is the only substance examined which stimulated a flow of pepsin. The emptying time of the stomach is less with meat extracts than with whole meat. Bovril reduces the time by 60% as compared with beef powder.—W. R. Boon, *Brit. med. J.*, ii/1937, 412.

**Meat juice** is the fluid portion of muscle fibre obtained by pressure or otherwise and may be concentrated at a temperature below the coagulation point of the soluble proteins.

**Beef and Malt Wine.** Extract of beef 4 oz., extract of malt 8 oz., port wine 1 gallon (*Ph. Form.*): or a meat juice and liquid extract may be used instead of the solid extracts.

"The Chemistry of Flesh Foods and their Losses on Cooking," by R. A. McCance and H. L. Skipp. *Spec. Rep. Ser. med. Res. Coun., Lond.*, No. 187, 1933.

**"Allenburys" Beef Juice** (*Allen & Hanburys, London*).

Fresh beef is expressed and the juice concentrated *in vacuo*. It retains the vitamins present in beef and contains iron and copper.

**Bovril** (*Bovril Ltd., London*).

A combination of beef extract and finely powdered beef fibrin and albumen, used as a substitute for ordinary beef tea.

**Brand's Meat Juice** (*Brand, London*).

A teaspoonful in a wineglassful of water is a useful tonic. Is prepared by cold process resulting in retention of full activity of juice of the raw beef.

**Eatan** (*British Amino Products, Surbiton; Fassett & Johnson, London*).

An essence of beef, described as a liquefied form of liver and animal proteins.

**Essence of Beef** (*Brand, London*).

A soft, transparent, amber-coloured jelly, prepared from beef by exhausting with tepid water.

**Ferrocarnis** (*Brand, London*).

*Dose.*—One teaspoonful in water thrice daily with meals.

Described as a flavoured solution of iron in organic combination with concentrated raw meat juice. An iron tonic food.

**Somatose** (*Bayer Products, London*). Water-soluble meat albumoses.

*Dose.*—2 to 4 teaspoonfuls daily dissolved in water. **Iron-Somatose** contains 2% iron.

**Trophonine** (*Reed & Carnrick, Jersey City; Coates & Cooper, London*).

Tonic food prepared from beef, malt, barley, milk and cocoa and containing 19.5% v/v of alcohol.

**Valentine's Meat-Juice** (*Valentine's Meat-Juice Co., Richmond, Va.*)

Meat juice obtained in a state ready for immediate absorption. One teaspoonful to be dissolved in warm or cold water.

**Albumen** (*B.P.C.*). *Syn.* EGG ALBUMEN, WHITE OF EGG. The liquid white of the egg of *Gallus bankiva* var. *domesticus* (*Gallinæ*). A nearly colourless or pale yellow fluid contained in a fibrinous network broken up by beating. Sp. gr. about 1.045. Contains 12% of protein, and is coagulated on heating to about 70°, or by adding alcohol. Is used as an antidote to poisoning by soluble salts of mercury and other heavy metals, and is an effective first-aid treatment for burns.



**BURNS.** A simple and effective form of first-aid treatment for burns is the immediate application of white of egg (no attempt being made to clean the burnt area or to collapse blisters). For burns of the face no other dressing is needed, but for other areas patches of cellophane are placed over the burn and a light padding of cotton wool over these. Minor burns of the first two stages heal in a week or less, but should be protected for two weeks. Within a few seconds of application all pain ceases.—J. L. Aymard, *Brit. med. J.*, ii/1940, 168. This method is used extensively as a home remedy in Eastern Europe.—A. Freitag, *ibid.*, 206.

**Preparation of Egg Protein for the Treatment of Hæmophilia.** By incubating egg-white at 37° with potassium bromide for several days a substance can be prepared which, when added to blood *in vitro*, gives a clear, structureless gel which does not shrink. The substance was found of value in hæmophilia. It may be prepared as follows:—Potassium bromide 40 g., is thoroughly mixed with egg-white 200 ml., and the mixture incubated at 37° for three days; 200 ml. of water is added and then 6 vols. of alcohol 98%. The liquid is filtered, and to the filtrate an equal volume of acetone is added to precipitate the active material. The precipitate is warmed at 70° with 20% nitric acid, neutralised with potassium hydroxide, and concentrated *in vacuo* at 70° to one-twentieth of its volume. Alcohol 98% is then added to the original volume, potassium nitrate is filtered off, the filtrate again concentrated *in vacuo* at 70° to one-twentieth of its volume, and a mixture of equal parts of alcohol and ether is added until no more yellow precipitate forms. The clear solution is concentrated until free from alcohol and ether, and the cloudy solution then remaining is allowed to stand for 24 hours, filtered, and the active material crystallised from the filtrate by further concentration. The substance is administered by intravenous or intramuscular injection of an aqueous solution, the usual dose being 10 to 30 mg. Much larger quantities were given without the production of local or general intravascular clotting. Repeated injections are necessary. A derivative of mucic acid was found to have similar properties.—W. A. Timperley, A. E. Naish and G. A. Clark, *Lancet*, ii/1936, 1142.

#### **Albumen Siccum (P. Ned. V).**

Yellowish, transparent, horn-like flakes obtained by evaporating white of egg at not exceeding 50°.

**Albumin Water,** for infantile diarrhoea and invalids in general. White of 1 egg mixed with sterile water 8 oz., sodium chloride 5 gr. or *q.s.* and a little whisky or brandy added.

**Ovi Vitellus,** yolk of egg, has a slightly alkaline reaction and consists of about 50% of water and 20% of oil emulsified by about 7% of lecithin and 15% of vitellin. An emulsifying agent giving emulsions not readily broken by acids or other electrolytes.

#### **Hæmoglobinum (B.P.C.).**

**Dose.**—5 to 30 grains (0.3 to 2 g.) or more.

The principal constituent of red blood corpuscles. Is supplied commercially in reddish-black powder or in scale form consisting of the oxygen compound, oxyhæmoglobin. Is a combination of the protein, globin, with hæmatin,  $C_{34}H_{39}O_4N_4Fe \cdot OH$ ; pure hæmoglobin contains about 0.34% Fe, 16% N and 0.6% S. May be given according to condition in cachet, capsule, or mixed with wine. It is used in secondary anæmia as a substitute for iron salts, which are more irritant to the stomach. Hæmoglobin solution gives a characteristic absorption spectrum. *Cf.* Vol. II for estimation in the blood and further details.

In the arterial circulation, hæmoglobin is present as oxyhæmoglobin (brilliant red in colour) the oxygen of which is given up to the tissues in its course, returning de-oxygenated (dark red) to the lungs by the venous system, where it is ready to take up fresh oxygen and so continue the process.

**Elixir Hæmoglobini (B.P.C.).** **Dose.**—1 to 2 drachms (4 to 8 ml.). Contains 10% *w/v* of hæmoglobin (about 5½ gr. per drachm). A pleasantly flavoured preparation of hæmoglobin as hæmatin.

**Hemoplas** (*Lumière, Lyons; Anglo-French Drug Co., London*). "Hæmoglobin in its natural state." Supplied in ampoules and dragées. In anæmia, hæmorrhage, tuberculosis, etc.

**Chlorophyll** (*B.P.C.*). The green colouring matter of plants extracted first by ether, then alcohol—in which latter the chlorophyll is soluble, leaving the waxy matter behind, or it can be produced by acetone extraction. It is supplied commercially in solid extract and liquid form, and is employed principally for colouring fats, oils, soaps, etc. Oil soluble, alcohol soluble and water soluble varieties are available. Oil soluble chlorophyll is obtained by diluting the purified extract with a fat, alcohol soluble chlorophyll is obtained by dilution with castor or other oil, and the water soluble variety by the action of dilute alkalis on the purified extract. Is stated to possess blood-forming properties, especially in conjunction with iron.

Chlorophyll contains no iron in itself but bears some close relation to iron for it cannot be formed in a plant from which iron is excluded. It contains magnesium, and perhaps this supplies to the component parts of chlorophyll the same cement which iron is said to give to the hæmoglobin molecule. Phylloporphyrin,  $C_{41}H_{54}N_4O$ , one of the decomposition products of chlorophyll, has a close relationship to hæmatoporphyrin,  $C_{41}H_{52}N_4O_2$ , an iron-free decomposition product of hæmoglobin. Going a stage further, hæmopyrrol,  $C_8H_{13}N$ , can be obtained from both.

### Medulla Rubra (*B.P.C.*).

*Dose*.—20 to 40 grains (1.3 to 2.6 g.).

The mixed fatty material from the bones of calves and young oxen. Contains erythroblasts from which the hæmoglobin-containing cells of the blood are developed. The bone marrow of older animals is yellow and contains no erythroblasts. Has been used in secondary anæmia, in leukopænia and in agranulocytic angina.

**ANÆMIA.** Desiccated red bone marrow and spleen, in equal proportions, given thrice daily in 5-grain doses, gave very definite improvement in 41 out of 46 cases of secondary anæmia. Treatment continued for 6 or 8 weeks.—*Brit. med. J. Epit.*, i/1925, 17.

**LEUKOPENIA.** Four patients with leukopenia and six with agranulocytic angina were treated with a yellow bone marrow concentrate *per os*; all recovered. Those with acute leukopenia showed clinical and hæmatologic improvement at the end of 40 to 48 hours. It is concluded that the yellow bone marrow concentrate contains a substance or substances which act to stimulate the maturation or liberation of leucocytes of the granulocyte series.—C. M. Marberg and H. O. Wiles, *Arch. intern. Med.*, 1938, 408.

**PULMONARY TUBERCULOSIS** improved by treatment with spleen extract and bone marrow, which definitely increased production of erythrocytes and hæmoglobin.—*Per J. Amer. med. Ass.*, ii/1925, 1513.

**Extractum Medullæ Rubræ** (*B.P.C.*). *Syn.* GLYCERIN EXTRACT OF RED BONE MARROW. *Dose*.—1 to 2 drachms (4 to 8 ml.).

1 in 4, in glycerin and chloroform water.

**Virol** (*Virol Ltd., London*). A preparation of bone marrow with malt, egg, and lime. Has nutrient properties for infants.

**Bynотone** (*Allen & Hanburys, London*). A combination of halibut-liver oil, bone marrow, yeast extract, hæmoglobin, malt extract and vitamin D. In malnutrition, pregnancy and convalescence.

**Roboleine** (*Oppenheimer, London*). A combination of bone marrow, malt, egg yolk, and lemon-juice. In wasting diseases.

## PHENACETINUM

*B.P., P. Helv. V, P. Belg. IV, P. Ned. V, etc.*

$\text{CH}_3\text{CO}\cdot\text{NH}\cdot\text{C}_6\text{H}_4\cdot\text{OC}_2\text{H}_5[\text{CH}_3\text{CO}\cdot\text{NH}:\text{OC}_2\text{H}_5 = 1:4] = 179\cdot1$ .

*Syn.* ACETPHENETIDIN, ACETPARAPHENALIDE, ACETOPHENETIDINUM (*U.S.P. XI*), ETHOXYPARA-ACÉTANILIDE (*Fr. Cx.*), ACETYL-PHENETIDIN (*P. Ital. V*), FENIDINA, FENINA (*F.E. VIII*).

*Dose.*—5 to 10 grains (0·3 to 0·6 g.), in cachets, tablets, or suspended in mucilaginous fluids. *P.G. VI* has max. single dose 15 grains; max. during 24 hours 45 grains, approx.

An acetyl compound of phenetidin,  $\text{C}_6\text{H}_4(\text{NH}_2)\text{OC}_2\text{H}_5$  (the ethyl ether of *p*-aminophenol). It is analogous to acetanilide (antifebrin). White, shining, laminar, tasteless crystals, m.p.  $134^\circ$  to  $136^\circ$ .

*Soluble* sparingly in water, about 1 in 1700, 1 in 70 of boiling water, 1 in 21 of alcohol 90%; also soluble in ether, chloroform, glycerin, and in sulphuric acid without colour.

Does not liquefy with sodium salicylate, but phenazone does, e.g., phenacetin 10 gr., caffeine citrate 2 gr., sodium salicylate 5 gr., are not incompatible.

*Uses.* Reduces temperature and soothes pain, very rarely causes rash or cyanosis. Successful in rheumatism, neuralgia, migraine and hysteria. In first stage of influenza relieves headache and mitigates aching of limbs. The safest of the antipyretics.

Antipyretic effect of phenacetin is enhanced by magnesium oxide in proportions of phenacetin 2 : magnesium oxide 1. Probable synergistic action.—*J. E. Winter and co-workers, J. Pharmacol., 1930, 347.*

*Mist. Phenacetin. Co. (N.I.F.).* Phenacetin 5 gr., caffeine citrate 1 gr. compound powder of tragacanth  $7\frac{1}{2}$  gr., cinnamon water to  $\frac{1}{2}$  oz.

**Phenacetinum Effervescens** (*B.P.C.*).

*Dose.*—1 to 2 drachms (4 to 8 g.). About 1 in 20.

**Phenacetinum cum Caffeina Effervescens** (*B.P.C.*).

*Dose.*—1 to 2 drachms (4 to 8 g.). About 1 in 20 of phenacetin and 1 in 60 of caffeine citrate.

**Tabellæ Phenacetini** (*B.P.C.*) contain 5 gr. (0·3 g.).

**Tabellæ Phenacetini Compositæ** (*B.P.C.*).

*Dose.*—1 or 2 tablets. Phenacetin 4 gr. and caffeine 1 gr.

**Tabellæ Phenacetini et Caffeinae Citratis** (*B.P.C.*).

*Dose.*—1 or 2 tablets. Phenacetin 4 gr. and caffeine citrate 1 gr.

*Dr. Faivre's Cachets* (*P. Basset, Paris; Wilcox, Jozeau, London*). Contain oxyquinoline 0·2 g., phenacetin 0·3 g., and magnesium oxide 0·1 g. (They no longer contain amidopyrine).

**Lactophenin** (*Boehringer, Mannheim; Coates & Cooper, London*). Lactylphenetidin (*P.G. VI*) in  $7\frac{1}{2}$  gr. tablets. *Dose.*—1 tablet several times daily, maximum daily dose 75 gr. Febrile conditions, insomnia in children, rheumatism, neuralgia, migraine.

[**P1-81**] **Treutabs** (*Camden Chemical Co., London*). Tablets containing phenacetin 0·25 g., aspirin 0·125 g., codeine phosphate 0·01 g., Hornburg salt 0·07 g. *Dose.*—1 or 2 tablets—not more than 8 in 24 hours. Analgesic in all painful and febrile conditions.

**Phenocoli Hydrochloridum.** *Syn.* AMINOACETO-*p*-PHENETIDIDE HYDROCHLORIDE.  $\text{CH}_3(\text{NH}_2)\text{CO}\cdot\text{NH}\cdot\text{C}_6\text{H}_4\cdot\text{OC}_2\text{H}_5\cdot\text{HCl} = 230\cdot6$ .

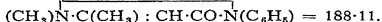
*Dose.*—8 to 15 grains (0·5 to 1 g.).

A white crystalline powder with sharp saline taste. Soluble about 1 in 16 of water.

An antipyretic resembling phenacetin in action, but more rapid in effect owing to greater solubility. It has been employed in rheumatic fever, malaria and influenza, and is stated to be of value in rheumatoid arthritis.

## PHENAZONUM

*B.P., U.S.P. XI, Fr. Cx., P.G. VI, P. Ned. V, P. Helv. V, P. Dan., etc.*



*Syn.* ANALGÉSINE, ANTIPYRIN, DIMETHYL OXYQUINIZINE, PHENYL-DIMETHYL-ISO-PYRAZOLONE, 1-PHENYL-2 : 3-DIMETHYL-5-PYRAZOLONE.

*Dose.*—5 to 10 grains (0·3 to 0·6 g.) in cachets, tablets or solution. *U.S.P. XI* average dose 5 grains. *Fr. Cx.* has max. single dose 2 g.; max. in 24 hours 8 g. Hypodermically 4 grains (0·25 g.) is painful. Has been given with cocaine hydrochloride  $\frac{1}{2}$  gr.

In white, crystalline, bitterish scales or powder, m.p.  $111^\circ$  to  $113^\circ$ . Gives a deep red colour with ferric chloride, nearly discharged by dilute sulphuric acid.

*Soluble* 1 in 1·2 of water, about 1 in 1·3 of alcohol 90%, 1 in 1·3 of chloroform, and 1 in 50 of ether.

*Incompatible* with spirit of nitrous ether, or other nitrites in the presence of free acid, an apparently inert bluish-green isonitroso-antipyrin being formed; also with the cinchona alkaloids, forming a precipitate which is soluble in weak acids.

Further, with phenol, tannic acid, iodine or mercuric chloride (precipitates); amyl nitrite, ammonia alum, hydrochloric acid, calomel, ferric chloride, ferrous and ferric sulphates, cupric sulphate, nitrous acid, sodium bicarbonate or orthoform.

Liquefies with butylchloral hydrate, betanaphthol and sodium salicylate, but solutions with the latter keep if dilute.

*Antidotes.* Treat as for poisoning by acetanilide, *see* p. 3.

**AGRANULOCYTOSIS.** In the recorded cases of agranulocytosis in which an analgesic drug has been suspected, an amidopyrine preparation has nearly always been held responsible. In view of the occurrence of cases following the use of Novalgin, it is important to bear in mind the possibility of antipyrin preparations being responsible when the causation of a case of agranulocytosis is under consideration. There are a number of proprietary preparations on the market containing antipyrin.—C. P. Donnison, *Brit. med. J.*, 1/1936, 84.

*Uses.* It is an analgesic and antipyretic, its action being rapid, more transient, and more toxic than phenacetin. In doses of 4 to 15 grains it relieves locomotor ataxy, chorea, migraine, facial neuralgia, dysmenorrhœa, rheumatism, sciatica and sea-sickness. It sometimes causes skin rashes and other untoward symptoms, but not so frequently as acetanilide. A solution applied locally is

hæmostatic. Local hæmorrhage of hæmophilia has been treated by application of a strong solution of phenazone in ferric chloride.

In middle-ear diseases, otitis media and inflammation of the tympanum, and tympanic membrane, a 5% solution in glycerin has been used by instillation.

GLOSSOPHARYNGEAL NEURALGIA well treated by phenazone and gelsemium. —J. P. Martin, *Brit. med. J.*, i/1931, 533.

SCIATICA. The following relieves the painful symptoms:—Phenazone 6 gr., phenacetin 3 gr., methylacetanilide  $1\frac{1}{2}$  gr., potassium sulphate  $1\frac{1}{2}$  gr., Dover's powder (*sine ipecacuanha*) 3 gr. To be given in a cachet 3 or 4 times in the 24 hours. Good effects are also obtained from the following:—Phenazone 5 gr., phenacetin 5 gr., opium powder  $\frac{1}{2}$  gr., in a cachet; 3 to 6 of which can be taken each day.

Phenazone (4 g. in 10 ml. of water with a little procaine hydrochloride) by perineural injection also alleviates pain.

If there is not prompt improvement following rest in bed and the administration of sedatives such as aspirin, amidopyrin and antipyrin, local injections of a 25% solution of antipyrin in alcohol may be used with benefit. Two or three ml. of the solution are injected at two or three points along the painful portion of the sciatic nerve. To avoid the alcohol reaching the nerve, a needle through which 1 ml. of 1% novocaine has been injected is then withdrawn at least 4 cm.—J. Paraf, per *Practitioner*, i/1937, 783.

Mist. Phenazon. Co. (N.I.F.). Phenazone 5 gr., potassium bromide  $7\frac{1}{2}$  gr., solution of burnt sugar 5 m., sodium salicylate 5 gr., aromatic solution of ammonia 15 m., water to  $\frac{1}{2}$  oz.

Phenazonum Effervescens (B.P.C.). *Syn.* EFFERVESCENT ANTIPYRIN. *Dose.*—1 to 2 drachms (4 to 8 ml.). About 1 in 12.

Phenazonum cum Caffeina Effervescens (B.P.C.). *Dose.*—1 to 2 drachms (4 to 8 g.). Contains about 1 in 12 of phenazone and 1 in 60 of caffeine.

Phenazoni et Caffeina Citras. *Syn. and Prop. Name.* ANTIPYRIN CAFFEINO-CITRICUM (*P. Austr.*, *P. Helv.* V and *P. Ned.* V), MIGRÆNINUM (*P. Jap.* V), MIGRAININE (*Bayer Products, London*).

*Dose.*—8 to 15 grains (0.5 to 1 g.). Contains phenazone 90%, caffeine 9% and citric acid 1%. Soluble 1 in 2 of water.

Incompatibles as phenazone *q.v.* Is serviceable in headache, but apt to cause sleeplessness.

Pommade Antiseptique Composée à l'Iodoforme (*Fr. Cx.*). *Syn.* POMMADE DE RECLUS. Phenazone 25, mercuric chloride 0.1, phenol 2.5, salol 6, iodoform 5, boric acid 15, alcohol 60% 15, soft paraffin 1000. The formula is often modified; it may be diluted or made stronger. For burns [P1] 1.2% of orthocaine may be added.

Tabellæ Phenazoni (B.P.C.). Contain 5 gr. (0.3 g.).

Phenazoni Acetylsalicylas. *Syn.* ANTIPYRIN ACETYLSALICYLAS.  $C_{11}H_{12}ON_2 \cdot CH_3 \cdot CO_2 \cdot C_6H_4 \cdot COOH = 368.2$ .

*Dose.*—8 to 15 grains (0.5 to 1 g.).

A white crystalline powder, soluble 1 in 160 of water, but about 1 in  $3\frac{1}{2}$  of alcohol 90%. Analgesic, antipyretic and anti-arthritis, used in sciatica, influenza, etc.

Phenazoni Salicylas (B.P.C.). *Syn.* ANTIPYRINUM SALICYLICUM (*P. Austr.*, *P. Belg.*, *Fr. Cx.*, *P. Helv.* V, *P. Dan.*, *P. Jap.*, *P.G. VI*, *P. Ned.* V), SALIPYRIN, PYRAZOLONUM PHENYLDIMETHYLICUM-SALICYLICUM.  $C_{11}H_{12}ON_2 \cdot C_6H_4(OH)(COOH) = 326.2$ .

*Dose.*—5 to 20 grains (0.3 to 1.2 g.). Max. single dose 2 g.; max. in 24 hours 6 g.

CC\*

A white crystalline powder, with sweetish taste, soluble 1 in 240 of water, 1 in 4 of alcohol 90%, and in ether and chloroform; incompatible with acids, alkalis and nitrites.

Useful in acute rheumatic fever and in chronic rheumatism, and sciatica; also for influenza and acute catarrh; as antipyretic in dose double that of phenazone.

**Dismenol** (*Roberts, London*). Tablets containing *p*-sulphamidobenzoic acid 0.05 g., phenazone 0.25 g., lactose 0.25 g. *Dose*.—1 tablet 2 or 3 times a day. For dysmenorrhœa.

**Saridone** (*Roche Products, Welwyn Garden City*). Tablets containing phenyldimethylisopropylpyrazolone  $1\frac{1}{2}$  gr., phenacetin  $2\frac{1}{2}$  gr., caffeine  $\frac{1}{2}$  gr. *Dose*.—1 to 3 tablets 3 or 4 times daily. Analgesic and antipyretic.

**Sedonan** (*Napp, London*). 5% solution of phenyldimethylpyrazolone in glycerin. For instillation in otitis media, otalgia and other inflammatory ear conditions.

**Spasmolyth** (*Warwick Pharmacals, Coventry*). Powders for the relief of asthma containing phenapyrine-caffeine 0.5 g. (a condensation product of phenazone 0.275 g., phenacetin 0.125 g., and caffeine 0.1 g.), phenyldimethylpyrazolone 0.45 g., codopyrine 0.03 g., extract of grindelia 0.01 g., cereus grandiflorus 0.01 g. *Dose*.—1 to 3 powders daily, one hour after meals; to be taken for several weeks.

[P1-81-84] **Amidopyrina** (*B.P.*). *Syn. and Prop. Name*. 4-DIMETHYLAMINO-1-PHENYL-2 : 3-DIMETHYL-5-PYRAZOLONE (*Fr. Cx.*), DIMETHYLAMINOPHENAZONE, PHENYLDIMETHYLDIMETHYL-AMIDOISOPYRAZOLONUM (*P. Ital. V*), DIMETHYLAMINOANTIPYRINUM (*P. Helv. V, P. Dan.*), AMINOPYRINA (*U.S.P. XI*), AMIDOFEBRIN, PYRAMIDON (*Bayer Products, London*).  $C_{11}H_{11}(N[CH_3]_2)_2N_2O = 231.2$ .

[P1], [81] and [84] "*Amidopyrine; its salts.*"

*Dose*.—5 to 10 grains (0.3 to 0.6 g.). *P. Helv. V* max. per day 15 grains. *U.S.P. XI* average dose 5 grains.

A white powder with m.p. 108°. Soluble about 1 in 18 of water and 1 in 2 of alcohol 90%; readily soluble in ether, chloroform and benzene.

**Incompatible** with amyl nitrite, apomorphine, acacia and oxidising agents.

**Antidotes.** Treat as for poisoning by acetanilide, *see* p. 3.

**Toxic Effects.** The prolonged use of amidopyrine, or its use in susceptible persons, may give rise to agranulocytosis, a condition characterised by a marked fall in the leucocyte count, pyrexia, severe pharyngitis and ulceration of the mouth and throat, marked prostration, and a rapidly fatal outcome in the majority of untreated cases. It should therefore be used with extreme caution, especially in analgesic mixtures, and its employment should be *immediately* stopped on the first signs of intolerance, *e.g.*, weakness, exhaustion, pyrexia, pharyngitis, and a tendency to sleepiness. Its use is best avoided entirely in elderly persons and in those suffering from severe and long-continued ill-health.

172 cases cited in which the illness has definitely followed the use of these substances.—R. R. Kracke and F. Parker, *J. Amer. med. Ass.*, ii/1935, 960.

Since May 1933 no less than 128 cases have been reported in which agranulocytosis developed after therapeutic doses of amidopyrine; 70 of them were fatal.—F. Plum, *Lancet*, i/1935, 14.

Barbiturates inhibit the acute toxic actions of amidopyrine, but not the chronic toxic effects. The combination of amidopyrine with barbiturates appears thus to possess certain peculiar dangers, because the latter are likely to mask any immediate effects of overdosage with amidopyrine.—Danielopolu and co-workers, *Brit. med. J.*, ii/1935, 1108.

In 26% of cases of aggranulocytic angina the disease followed the administration of amidopyrine or allied drugs. That in these instances the disease may have been actually caused by the therapy is possible, perhaps probable. In another 30% of the cases the evidence shows that in spite of the fact that these drugs were taken in considerable quantities they definitely have no causative relation to the disease. Of these patients 44% received no drugs of this type whatsoever, yet their clinical and hæmatologic pictures were similar in every respect.—H. Jackson, *Amer. J. med. Sci.*, 1934, 188, 482.

The administration of large doses of amidopyrine to 103 patients (1 or 2 g. daily) over a prolonged period (40 days or more) caused no significant decrease in the number of leucocytes or granulocytes. The entirely negative results of this clinical experiment would seem to substantiate the widely held opinion that granulopenia, when associated with amidopyrine medication is a matter of individual susceptibility. Except in the presence of some predisposing factor, amidopyrine is probably incapable of causing granulopenia.—S. D. Simon and M. H. Metz, *J. Lab. clin. Med.*, 1936, 1154.

A dose of 30 grains of amidopyrine was given daily to each of 32 patients over periods extending from 2 weeks to 3 months and their granulocytic counts followed. There was no marked change in any of the counts. The absence of any ill effects may have been due to the following of a routine, i.e., withdrawal of the drug as soon as any symptoms of toxicity arise, such as indigestion, lack of appetite, dizziness, etc. It would seem that if this simple procedure were followed there would be no need of frequent blood counts. It seems unwarranted to condemn a drug which has been found useful for so many years without a definite and clear reason for so doing. Whether there is an individual susceptibility in the nature of an allergic reaction, or whether the cases are simply based on the law of chance association, must be determined.—J. S. Davis and L. F. Frissell, *J. Lab. clin. Med.*, 1937, 23, 107.

**Uses.** Amidopyrine is analgesic and antipyretic, resembling phenazone in its action, but being effective in smaller doses; its action is exerted somewhat more slowly and is of longer duration. It has been employed in acute pyrexial conditions and for the relief of pain in sciatica, neuralgia, migraine and dysmenorrhœa. It has also been advocated for use in measles (1 gr. for each year of age up to 5 gr., given 4-hourly until temperature drops), but the clinical evidence as to its value is conflicting.

**INFLUENZA IN CHILDREN** well treated by giving a 3 or 4% solution. From birth to 1 month 0.05 g., 3 to 6 months 0.1 g., 6 to 12 months 0.15 g., 2 to 5 years 0.2 g. Given 2-hourly till temperature reached normal, then 3-hourly, then 4-hourly, and later 3 times daily. No unpleasant symptoms and temperature fell after third or fourth day.—G. Petrányi, *Amer. J. Dis. Childh.*, Dec., 1933, 1011.

**RHEUMATISM.** Investigation on a series of 1000 patients as to the value of amidopyrine combined with physiotherapy in rheumatic conditions. 500 patients received physiotherapy alone, and the other 500 received physiotherapy plus 2 to 3 grammes of amidopyrine a day for 6 weeks. No advantage was detected from the addition of amidopyrine to the physiotherapeutic measures.—K. E. Rotschuh and M. Benard, *Klin. Wschr.*, 1936, 1838.

[P1-S1-84] **Tabellæ Amidopyrinæ** (B.P.C.) contain 5 gr. (0.3 g.).

[D-P1-S1-84] **Tabellæ Amidopyrinæ Composita** (L.H.). Amidopyrine 4 gr., acetylsalicylic acid 5 gr., diamorphine hydrochloride  $\frac{1}{16}$  gr., carmine q.s. in 1 tablet.

[P1-S1-84] **Amidopyrinæ Salicylas.** White crystals. Analgesic for neuralgia and rheumatism. Tablets contain 5 gr.

[P1-S1-84] **Amidophen** (Lilly, London). Capsules containing amidopyrine  $3\frac{1}{2}$  gr., phenacetin 1 gr., caffeine  $\frac{1}{2}$  gr., and dry hyoscyamus extract  $\frac{1}{2}$  gr. Analgesic, sedative and antipyretic.

**Causyth** (*Josper Ltd., London*). The cyclohexatrienepyrindinesulphonate of a pyrazolone derivative, available in powder form or as tablets containing  $7\frac{1}{2}$  gr. or suppositories containing 15 gr. Antirheumatic, antipyretic and analgesic. *Dose*.—1 to 4 tablets three times a day or, as an enema, 45 to 90 gr. in 50 ml. of water.

[P1-S1-S4] **Compral** (*Bayer Products, London*).  $\frac{7}{8}$ -gr. tablets containing amidopyrine combined with trichlorethylurethane for use in dysmenorrhœa and pain generally. *Dose*.—1 or 2 tablets 3 times daily before meals. A rapidly acting, mildly sedative analgesic.

[P1-S1-S4] **Gardan** (*Bayer Products, London*). A combination of amidopyrine and Novalgin in 5-gr. tablets. *Dose*.—5 grains (1 tablet) 2 or 3 times daily as an antipyretic and analgesic.

**Novalgin** (*Bayer Products, London*). Sodium phenyldimethylpyrazolon-methylaminomethanesulphonate in 5-gr. tablets. *Dose*.—1 tablet 3 or 4 times daily after meals, with water.

An amidopyrine derivative introduced as an anti-rheumatic, stated to be better tolerated and more effective than salicylates, for use in articular and muscular rheumatism, sciatica, polyarthritis, and lumbago.

An injection of 1 to 2 ml. of 50% Novalgin solution, available in ampoules, is also given as an analgesic.

[P1-S1-S4] **Sinepan** (*Richter, London*). Amidopyrine 3 gr., codeine hydrochloride  $\frac{1}{2}$  gr., narcotine hydrochloride  $\frac{1}{2}$  gr. *Dose*.—1 when indicated. Substitute for morphine and opium preparations.

**Triamid** (*Richter, London*).  $\alpha$ -Acetyl- $\beta$ -methyl- $\beta$ -dimethyloxamide- $\beta$ -phenylhydrazine (dioxamidopyrine), an analgesic, antipyretic and sedative stated to have negligible toxicity. M.p. 37°, soluble in water (1 in 3), more soluble in the presence of salicylates and benzoates. Available in tablets containing  $\frac{1}{2}$  or 5 gr. *Dose*.— $1\frac{1}{2}$  to 10 grains thrice daily.

[P1-S1-S4] **Trigemin** (*Bayer Products, London*). Combination of amidopyrine and butylchloral hydrate. *Dose*.—0.25 to 0.5 g. Analgesic.

## PHENOL

B.P., U.S.P. XI, Fr. Cx., P. Dan., P. Helv. V.

$C_6H_5 \cdot OH = 94.05$ .

*Syn.* ACIDUM CARBOLICUM; PURE CARBOLIC ACID, PHENYL HYDRATE, BENZOPHENOL (P. Belg. IV), FENOL (F.E. VIII).

[P1] "Phenols (any member of the series of phenols of which the first member is phenol, and of which the molecular composition varies from member to member by one atom of carbon and two atoms of hydrogen) except in substances containing less than 60%, weight in weight, of phenols; compounds of phenol with a metal, except in substances containing less than the equivalent of 60%, weight in weight, of phenols."

[P2] "Phenols as defined in Part I of this List (see [P1] above) in substances containing less than 60%, weight in weight, of phenols; compounds of phenol with a metal in substances containing less than the equivalent of 60%, weight in weight, of phenols."

[S3] "Phenols—in Carvacrol; creosote obtained from coal tar; essential oils in which phenols occur naturally; medicines containing less than 1% of phenols; nasal sprays, mouth-washes, pastilles, lozenges, capsules, pessaries, ointments, or suppositories containing less than 2.5% of phenols; smelling bottles; soaps for washing; solid substances, other than pastilles, lozenges, capsules, pessaries,



ointments and suppositories, containing less than 60% of phenols; tar (coal or wood), crude or refined; tertiary butyl cresol; thymol."

[86] "Phenols—specify proportion as the proportion of phenols (added together) contained in the preparation."

"Compounds of phenol with a metal—specify as the proportion of phenols (added together) that the preparation would be calculated to contain on the assumption that the compounds of phenols with a metal had been wholly converted into the corresponding phenols."

Dose.—1 to 3 grains (0.06 to 0.2 g.). Fr. Cx. max. single dose  $1\frac{1}{2}$  grains; max. during 24 hours  $4\frac{1}{2}$  grains approximately. U.S.P. XI average dose 1 grain.

In colourless crystals or agglomerated masses liable to become pink on keeping unless stored in a cool place and protected from light. M.p.  $39^{\circ}$  to  $40^{\circ}$ .

**Solubility.** 100 parts are liquefied by 10 of water, form a clear liquid with 30 to 40 of water, and are completely dissolved by 1300 of water. Also soluble  $3\frac{1}{2}$  in 1 of glycerin, 3 in 1 of chloroform (nearly), 1 in 2 of olive oil, 5 in 1 of ether,  $\delta$  in 1 of alcohol (90%),  $2\frac{1}{2}$  in 1 of benzene, 4 in 1 of acetic acid and 1 in about 20 of soft paraffin.

1% of phenol in liquid paraffin forms a saturated solution. More will dissolve warm but is thrown out again on cooling. It was thought that the addition of menthol might form a non-escharotic compound, and hence alleviate the effect of the phenol, but this is erroneous.

**Incompatible** with alkaline salts, acetanilide, phenazone, quinine salts, phenacetin and iron salts. Mixtures of phenol with camphor, chloral hydrate, menthol or thymol liquefy.

A solution of lead subacetate gives a precipitate with phenol, but there is no change with the acetate. Other phenols, cresols, etc., do likewise, except pyrogallol. The precipitate may be prevented by adding a trace of acetic acid to the subacetate solution.—G. A. Medley, *Pharm. J.*, ii/1926, 149.

The precipitate formed is apparently of the formula  $\text{Pb}(\text{O}\cdot\text{C}_6\text{H}_5)_2\cdot\text{Pb}(\text{OH})(\text{O}_2\text{C}\cdot\text{CH}_3)_2$ .—E. A. Lum, *ibid.*, i/1929, 149, 251; J. E. Driver, *ibid.*, 251; see also E. Matthews, 297 and E. H. Lane, 321.

**Antidotes.** Give emetic (not always effectual). Empty stomach by stomach tube, using 2 oz. of magnesium sulphate or sodium sulphate in 2 gallons of water. Give 1 oz. of magnesium sulphate in 1 pint of water to be retained. Demulcents, such as white of egg, mucilaginous drinks; do not give alcohol, oils, fats or glycerin. Keep patient warm. Artificial respiration and oxygen inhalation if necessary. Strychnine,  $\frac{1}{8}$  gr., hypodermically. Saline infusion.

Case of phenol poisoning recovered after successive aspiration of stomach and gastric lavage with saline, diluted egg albumen and 50% alcohol respectively; caffeine and adrenaline given as stimulants; glucose and saline intravenously; 40 ml. of 1% methylene blue solution intravenously. Suggested that this may have influenced favourable outcome.—W. M. Sheppe, *Milit. Surg.*, 1935, 76, 30.

**Inhalation of fumes of carbolic acid** caused grave poisoning symptoms. Intravenous saline, 2 pints, with addition of 2 drachms of sodium bicarbonate saved life. Breathing (assisted by the use of oxygen) improved at once.—R. Eccles Smith, *Lancet*, ii/1922, 1359.

Absorption of crude carbolic acid through the skin with fatal result. A bottle broke in a man's pocket on his journey home by train—extensive burning of hip, thigh and scrotum. Ultimate death.—W. R. M. Turtle and T. Dolan, *Lancet*, ii/1922, 1273.

Liquefied phenol, instead of a dilute solution, was applied by mistake as a dressing for neuritis in the arm. The patient died.—per *Analyst*, 1939, 679.

**Uses.** Externally phenol is employed for its antiseptic and deodorant properties, and a 5% solution is widely employed for the disinfection of utensils, instruments, hands, etc. Strong solutions are irritant and caustic and are seldom used, though the pustules of acne and small-pox may be treated by evacuating the contents and applying the smallest possible quantity of a mixture of phenol and camphor equal parts. Carbolic camphor (25%) has been employed as a paint to the cervix uteri, and for the relief of pain in toothache, and a mixture of equal parts of phenol and collodion has also been employed for the latter purpose. When applied to the skin in weak or moderately strong solutions (1 or 2%) phenol produces local anæsthesia, and this, combined with its antiseptic action, encouraged its use as a wound dressing. Unfortunately it is absorbed from the skin and mucous membranes and its prolonged use may give rise to toxic symptoms; in particular, solutions of phenol should not be applied as dressings to the fingers or toes, since gangrene may result. A 1% lotion may be employed, however, with benefit for its antipruritic effect in the relief of itching skin affections. For use as an antiseptic mouth-wash or gargle, or as a nasal and pharyngeal spray (e.g., in acute coryza) it is employed in a  $\frac{1}{2}$  to 1% aqueous solution. Similar strength solutions are also of value as a vaginal injection in leucorrhœa and uterine ulceration. Phenol also has a powerful antizymotic action, and may be used either as a lotion or an ointment in the treatment of parasitic skin diseases such as ring-worm, sycosis, pityriasis, eczema, pediculosis capitis, etc.

The presence of glycerin retards the local action of phenol, and a solution of phenol in glycerin is almost non-caustic and only slightly toxic, and is employed as a paint in inflammatory conditions of the mouth and throat, for infections of the external auditory meatus and for otitis media.

Phenol has been employed by *injection* for its sclerosing action (2 to 4 m. of undiluted liquefied phenol) in varicose veins, hæmorrhoids, and rectal prolapse (5% phenol in almond oil); chronic hydrocele has been treated by injection into the sac of iodised phenol; and a 5% solution of phenol has been successfully employed in the treatment of anthrax, injections being made underneath and round the pustules.

Internally, in small doses, phenol stimulates the gastric secretions and has a carminative action. In 2 minim doses it has been found of value in persistent vomiting and in gastritis. It is of little value as an intestinal antiseptic owing to its prompt absorption and marked toxicity.

**ANTHRAX.** 1 to 2 ml. of 5% phenol beneath and round the pustule effects complete and dramatic cure. Cheap and painless and all except severe cases treated as out-patients.—G. C. Dorling, *Brit. med. J.*, i/1932, 123.

Inject 2 to 3 ml. of 5% phenol in 2 to 4 places around and into the base of the pustule; if very large 5 ml. may be needed. Merely a simple dressing is then applied. If, on the following day, there are any signs of the pustule progressing, a further injection is made at that site, but often only one injection is required. Within 48 to 72 hours the pustule dries up and in 7 to 10 days the centre separates, but unless an excess of carbolic has been used the scar is usually quite small. Of 16 cases 2 died, and they were in an advanced stage.—G. C. Dorling, *Chinese med. J.*, 1935, 662.

**HERNIA; INJECTION TREATMENT.** Good results are reported from the use of the following solution:—Phenol 30, alcohol 15, tincture of thujæ 15. The dose is 4 to 8 m., and an average duration of treatment is 8 to 12 injections which should be given once or twice weekly.—W. McMillan and D. Cunningham, *J. Amer. med. Ass.*, 1/1936, 1791. (See also Obrutatin, p. 810).

**TETANUS** treated by intrathecal injections. Phenol kills tetanus toxin in vitro. 1 in 400 solution employed—30 to 40 ml. for adults. 10 out of 14 cases recovered.—S. Suvansa, *Lancet*, 1/1931, 1075.

**VARICOSE VEINS.** Injection of undiluted liquefied phenol 2 to 4 minims preferable to quinine-urethane, sodium salicylate, etc., which give rise to considerable pain and are dangerous in cases of idiosyncrasy. The carbolic acid is at once locked up in the clot, which forms immediately. 4 minims is sufficient to obliterate a large varicose saphenous vein. The injection is practically painless and the vein almost immediately hardens. Four to eight veins may be injected at a sitting. Veins do not become immunised to the acid.—P. P. Dalton, *Brit. med. J.*, ii/1928, 1037.

**VOMITING.** Immediate and dramatic effect in a case of persistent and uncontrollable vomiting in a case of uræmia, following a 2-minim dose of phenol. Phenol is a gastric sedative of great value, and is of benefit in many cases of gastritis and, used with morphine, gives astonishing relief in inoperable carcinoma of the stomach.—J. C. Lyth, *Brit. med. J.*, ii/1935, 903.

**WOUNDS.** Wounds received in the Spanish Civil War were first cleansed with a mixture of ether 1 part, and hydrogen peroxide 3 parts. Then a solution of phenol 4 g., camphor 3 g., thymol 2 g., glycerin 10 ml. in alcohol to 100 ml. was applied. In all cases injections of tetanus antitoxin and polyvalent gas gangrene sera were given.—S. Perez-Vazquez, *Pharm. J.*, ii/1939, 265.

**Carbasus Phenolis (B.P.C.).** *Syn.* CARBOLIC GAUZE. Contains 1 to 3% of phenol when freshly prepared.

**Gossypium Carbolisatum.** *Syn.* PHENOL WOOL.

To prepare this, impregnate absorbent cotton 1 under pressure with 1 of an ethereal solution (5%) of phenol. Spread out and dry rapidly. **Linteum Phenolis** is also prepared.

**Cataplasma Phenolis (B.P.C.).** 2% in linseed poultice.

**Colloidium Carbolisatum (B.P.C.).** A jelly consisting of equal parts of phenol and simple collodion. A local anæsthetic for application to decayed teeth.

**Collut. Pot. c. Phenol. (N.I.F.).** Solution of potassium hydroxide 2 dr., liquefied phenol 2 dr., solution of bordeaux B 40 m., water to 8 oz. 1 tablespoonful in  $\frac{1}{2}$  pint of warm water.

**Gargarisma Phenolis (B.P.C.).** Glycerin of phenol 5% v/v in water. For foul breath and sore throat.

**Garg. Phenol. Co. (N.I.F.).** Liquefied phenol 2 dr., solution of potassium hydroxide 2 dr., trypan blue  $\frac{1}{4}$  gr., water to 8 oz. 1 tablespoonful to  $\frac{1}{2}$  pint of warm water.

**[P2] Glycerinum Phenolis (B.P.).** *Syn.* GLYCERINUM ACIDI CARBOLICI.

*Dose.*—5 to 15 minims (0.3 to 1 ml.).

Phenol 16, glycerin 84. The preparation is *unnecessarily strong* for general local use. *Fr. Cx.* has 3% w/w. It is employed as a throat pigment and has been used in acute middle ear catarrh with good results. Carbuncles are well treated by applying pledgets soaked in the glycerol. As soon as pus shows, the

epithelium is turned back and the part may be later syringed out.

A solution of phenol in glycerin is almost non-caustic and only slightly toxic. *Caution (B.P.)*.—Dilution with water renders it caustic. It may be diluted with glycerin.

In the treatment of acute otitis media the glycerin of phenol of the *B.P.* is too concentrated and should be diluted with four to six volumes of glycerin, giving a concentration of 4 to 2½% of phenol.—F. C. Ormerod, *Practitioner*, i/1937, 522.

[P2] **Aurist. Phenol. (N.I.F.)**. Glycerin of phenol 3 dr., glycerin 5 dr.

For earache, a few drops, slightly warmed, are invaluable. This strength is ample.

[P2] **Injectio Phenolis et Olei Amygdalæ (C.X.H.)**. Phenol 20 gr., menthol 1 gr., almond oil to 1 oz. For periveneous injection in hæmorrhoids; 5 ml. can be injected around each of not more than two separate hæmorrhoids at a time.

[P2] **Carbolised Almond Oil**. Phenol 1, sterile almond oil to 20.

HÆMORRHOIDS well treated by injection of 1 to 2 ml. for each pile, under the mucous membrane, and injections continued at 5 to 7-day intervals until piles are of parchment-like hardness. Requires special instruments, skill, and experience.—A. S. Morley, *Lancet*, i/1928, 545. See also W. B. Gabriel, *Lancet*, i/1930, 162.

V. Meisen now adopts 5% phenol in almond oil.—*Lancet*, i/1931, 877.

W. S. Perrin uses phenol 1, glycerin 2 and water 2—usually a 5-minim dose.—*Lancet*, i/1929, 569. W. B. Gabriel uses 5% of phenol in almond oil—with usually 3-ml. dose—as also E. T. C. Milligan. Sir Charles Gordon Watson uses 15% phenol in glycerin and A. S. Morley 5% in oil.—*Brit. med. J.*, i/1931, 897.

If the vegetable oil be boiled for an hour and then filtered and the phenol added subsequently, the influenza-like symptoms which sometimes follow injection will not occur.—G. Sacks, *Brit. med. J.*, i/1933, 313.

The solution which is used at all the out-patient clinics at St. Mark's Hospital is 5% phenol in almond oil with 2 grains of menthol to 1 oz. (**Albright's Solution**). The ideal cases for injection are first-degree piles; a single small vascular pile can almost invariably be cured by a single injection; second-degree piles are less favourable, and third-degree piles are not suitable for injection. It is essential to use a sufficiently long proctoscope and to inject the phenol in oil into the submucous layer at the upper pole of the internal hæmorrhoids; no pain should be caused by the injection. The amount injected is usually 2 or 3 ml., and sufficient should be used to produce a smooth, rounded swelling in the submucous layer, slightly pale but not white. When a pile is particularly vascular and bleeds freely from its lower pole from 6 to 8 m. of 20% phenol in glycerin and water can be injected into the substance of the pile, either at the same time as the submucous injection high up or at a later session. Subsequent injections are given at weekly intervals.—W. B. Gabriel, *Brit. med. J.*, ii/1939, 1266.

The addition of menthol, as in Albright's Solution, has no advantages and sometimes gives rise to unpleasant side-effects. The injection treatment is equally suitable and satisfactory for third-degree piles (giving five weekly injections into each pile).—A. S. Morley, *Brit. med. J.*, i/1940, 72.

**COMPLETE RECTAL PROLAPSE** satisfactorily treated by carbolised almond oil, but injections should be given deeply enough to reach the muscular coat, the aim being to inject all round the rectal wall: usually 2 to 3 ml. is required, 4 or 5 injections being given at weekly intervals. Relapses are probable, but patients should be given the option of trying the injections before resorting to more drastic operations.—A. S. Morley, *Brit. med. J.*, ii/1934, 204.

[P2] **Obturatorin (Mayer's Formula)**.

Zinc sulphate 1 dr., phenol cryst. 6 dr., glycerin 4 dr., Aq. Cinnamomi 1 oz., fluid extract of *Pinus Canadensis* (dark) 5 dr., redistilled water 2 oz. Dissolve the zinc sulphate in the cinnamon water; liquefy the phenol by heating; add the glycerin, shake and cool. Add the distilled water and the *Pinus Canadensis* and shake. Allow to stand for a week, shaking daily. Filter. The solution is muddy when cold but becomes clear on heating. Boil before injection. For the injection treatment of inguinal hernia inject ½ ml. first injection and 1 ml. subsequently (15 to 20 being the average at 4 to 7-day intervals). Insert needle

vertically over site of internal ring till point is felt to pierce the aponeurosis: withdraw needle after every few drops to make sure the point is still outside any vessel. End-results compare favourably with operation. Patients not suitable for the treatment are those in which the hernia is not completely reducible or satisfactory fitting of a truss is impossible, active venereal disease or history of tuberculosis; in children, cases of hæmophilia.—St. G. B. Delisle Gray, *Brit. med. J.*, ii/1932, 13. "Obturatorin" is not a proprietary.—*Ibid.*, ii/1932, 385.

At the hernia clinic in the Minneapolis General Hospital, 1000 patients have been treated with this method without a death and in general with excellent results, but familiarity and skill in the use of injection methods is essential to success.—F. B. Bowman, *Canad. med. Ass. J.*, 1937, 277.

Twenty patients with hernias were treated by the injection method (Mayer's Solution in 11 cases, Synasol in 5, and Tripoli Suspension in 4) and carefully followed. At the end of four years two patients were cured. The injection treatment of hernias is not satisfactory and should be used only when the patient must not be operated on.—R. Slater, *New Engl. J. Med.*, ii/1939, 895.

[P2] **Liquor Phenolis Alkalinus (B.P.C.).** *Syn.* SOLUTION OF SODIUM PHENATE.

Phenol 10% w/v with sodium hydroxide and water. Diluted with 20 to 30 parts of water it is used as a mouth-wash.

[P2] **Phenol Sodique Dissous (Fr. Cx.).**

Phenol 100 g., sodium hydroxide solution 20 g. (30% by weight), water to 1000 ml. The sodium hydroxide in this is insufficient to combine with the phenol. The *Fr. Cx.* preparation, in fact, contains about 8.6 g. per 100 ml. of free phenol, only 1.4 of the total 10 g. being in the combined condition.

[P2] **Liquor Potassii Phenatis Compositus (B.P.C.).** *Syn.* LIQUOR POTASSII CARBOLATIS COMPOSITUS.

A flavoured preparation containing 5% v/v of liquefied phenol in alkaline solution.

[P2] **Liquor Sodii Phenatis Compositus (B.P.C.).** *Syn.* LIQUOR SODII CARBOLATIS COMPOSITUS, PHENOL SODA. A flavoured preparation containing 3% w/v of phenol as sodium phenate.

[P2] **Lotio Phenolis (B.P.C.).** *Syn.* CARBOLIC ACID LOTION.

1 in 80, coloured pink.

Carbolic ochromosis due to use of 5% phenol lotion as dressing to leg ulcers over 35 years.—J. L. Berry, *Lancet*, ii/1931, 124.

[P2] **Lotio Phenolis (R.L.O.H.).** *Syn.* LOTIO ACIDI CARBOLICI (R.L.O.H.).

Liquefied phenol 24 m., sterilised water at 50° to 1 oz. [P2] *N.I.F.* has liquefied phenol 2 dr., trypan blue  $\frac{1}{2}$  gr., water to 8 oz.

[D-P1-81] **Lotio Phenolis et Cocainæ.**

Phenol  $\frac{1}{2}$  dr., cocaine hydrochloride  $\frac{1}{2}$  dr., cherry laurel water 1 oz., rose water 3 oz. For pruritus.

In the later stage of treatment of chronic eczema a lotion containing phenol, Liquor Picis Carbonis, glycerin and spirit may be used as a stimulant to growth of healthier epidermis.

[P2] **Smith's Sterilising Solution.** Phenol 20, borax 5, glycerin 200, peppermint water 30, water to 1500 parts.

[P2] **Ravogli's Liniment.** Phenol 1, glycerin 2, alcohol 90% 16, rose water to 32. In skin affections.

[P2] **Oleum Carbolisatum (B.P.C.).** *Syn.* CARBOLIC OIL.

1 in 20, in arachis oil. For burns and scalds.

[P2] **Oleum Lubricans (B.P.C.).** *Syn.* LUND'S OIL, CATHETER OIL.

Phenol 5% w/v in castor oil and arachis oil. For oiling catheters. Carbolic catheter oil has no value.—O. S. Gibbs, *Brit. med. J.*, i/1931, 581.

**Surgical Lubricant** for catheters, etc.

Sarch 4, glycerin 35, add water  $8\frac{1}{2}$ ; heat to boiling, remove from flame and add boric acid in powder  $2\frac{1}{2}$ , warm to dissolve, and when nearly cold add phenol 1. The lubricant is non-greasy and does not attack rubber goods. It can be removed by water. It will not attack metal instruments if left in contact for a short time, but is not intended as a coating to store them in—for this, soft paraffin or liquid paraffin is best.

[P1] **Catheter Lubricant (Meltzer's Formula).**

Triturate tragacanth 3 with glycerin 20, add water 100, and sterilise, then add mercury oxycyanide 0.25.

See also *Pasta Tragacanthæ Composita*, p. 1003.

**Pastillus Phenolis** (Glycogelatin Basis).

Contains  $\frac{1}{2}$  grain (0.03 g.) phenol. Antiseptic and stimulant. For ulcers in the mouth or throat and for purifying the breath.

[P2] **Phenol cum Camphora (B.P.C.).** *Syn.* CARBOLIC CAMPHOR. Phenol 25% *w/v* with camphor.

Is not miscible with water or glycerin. Antiseptic and local anæsthetic, serviceable in toothache.

Ulcers produced by X-ray burns have been treated locally by a mixture of equal parts of phenol and camphor.

**Caution.** Not intended for extensive use. It is not suited for applying all over the face. Accidents have occurred.

[P1] **Phenol Iodisatum (B.P.C.).** *Syn.* IODISED CARBOLIC ACID, PIGMENTUM IODI CARBOLICUM.

Iodine 10% *w/v* in liquefied phenol.

[P1] **Acidum Carbolicum Liquefactum et Iodum (C.H.W.)** has iodine 1, liquefied phenol 4.

For intrauterine medication on cotton wool. Chronic discharging sinuses have been treated by 5 minutes' application of iodised phenol, also inoperable uterine carcinoma after curetting. Useful also for ringworm of the scalp.

CHRONIC HYDROCELE of the tunica vaginalis well treated by injection into the cavity of iodised phenol (4 parts of iodine to 2 parts of phenol); withdraw all fluid from the sac and, with the needle *in situ*, inject iodised phenol 3 minims for every ounce of fluid withdrawn. Massage scrotum for 5 minutes and apply collodion dressing. Patient rests in bed for 24 hours with scrotum supported on a pillow. Not more than 5 ml. should be given at one sitting. Better to commence with 2 ml.—Morton Whitley, *Brit. med. J.*, ii/1932, 241.

Carefully distinguish from:—

**Dilute Iodised Phenol Injection.** Lugol's solution 2.5, phenol 1, boiling water to 200. Much weaker than the preceding. Is used as a pigment in diphtheria, or as a gargle or inhalation. Is useful also as a nasal douche in ozæna and for intrauterine injection.

[P1] **Phenol Liquefactum (B.P.).** *Syn.* ACIDUM CARBOLICUM LIQUEFACTUM.

**Dose.**—1 to 3 minims (0.06 to 0.2 ml.). *U.S.P. XI* average dose 1 minim.

Contains 80% *w/w* of phenol. Sp. gr. about 1.063. The congealing point of liquefied phenol of this strength is  $3^{\circ}$ , and the trouble experienced with the *B.P.* '14 preparation (87% *w/w* of phenol) from crystallisation in cold weather is thus obviated. If cooled below the congealing point it should be completely melted before use. *Fr. Cx.*, *P. Belg. IV* and *P. Jap. V* have phenol 10, water 1; *P. Dan.* phenol 9, water 1; *P. Helv. V* phenol 85, water 15.

**[P1] Phenol Liquefactum (U.S.P. XI).**

*Average dose.*—1 minim (0.06 ml.). Prepared by liquefying phenol in its unstoppered container by heating in a water bath and adding 1 part by weight of water to 9 parts by weight of phenol.

**[P2] Soluté Antiseptique de Phénol Salicylé (Fr. Cx.).** *Syn.* PHENOSALYL.

Phenol 150 g., glycerin 100 g., sodium salicylate 18 g., sodium benzoate 3 g., menthol 0.5 g., water to 1000 g. 0.2 to 0.4% in conjunctivitis and 1% in eczema.

**[P2] Pigmentum Carbol-Fuchsin (St. T. H.).** Saturated solution of basic fuchsin 10 ml., phenol 5 g., boric acid 1 g., resorcinol 10 g., water 100 ml. Dissolve the phenol in the water, add the fuchsin solution, filter, add the boric acid, allow to stand for 2 hours and add the resorcinol. To be stored in the dark in a stoppered amber-coloured bottle.

**Pilula Phenolis.** *Syn.* PILULA ACIDI CARBOLICI.

Phenol 2, powdered liquorice 1, powdered althaea 1. In grains for 1 pill, in grammes for 15 pills.

**Resina Acidi Carbolic (R.D.H.).**

Colophony 4, phenol 4, chloroform 3. Dissolve and filter.

This is used as an obtundent and a temporary antiseptic filling. *Method.*—Syringe out all food from the cavity and remove as much decay as possible. Apply on a wool pledget to relieve toothache.

**Resina Carbolisata (B.P.C.).** Phenol 1, mastic 1, colophony 2, chloroform 1.

**[P2] Solutio Phenoli (I.A.)** contains 2% of phenol. *Aqua Phenolata (P. Helv. V, P. Jap. V)* is this strength.

**[P2] Solutio Phenolis et Glycerini (St. T. H.).** Phenol 48 gr., glycerin 2 dr., water to 4 dr. *Dose.*—2 to 5 minims paravenously. For hemorrhoids.

**[P2] Preservative Solution** for anatomical specimens.

Phenol 1, glycerin 4, methylated spirit 5.

**Stupa Phenolis (B.P.C.).** *Syn.* CARBOLISED TOW. Contains 5% of phenol when freshly prepared.

**[P2] Suppositorium Phenolis (B.P.).** *Syn.* SUPPOSITORIUM ACIDI CARBOLICI.

Unless otherwise stated, contains 1 grain (0.06 g.) of phenol in a 15-grain suppository. May be made with  $\frac{1}{2}$  grain of white beeswax and oil of theobroma *q.s.*

**[P2] Trochiscus Phenolis (B.P.).** *Syn.* TROCHISCUS ACIDI CARBOLICI. Contains  $\frac{1}{2}$  grain (0.03 g.) with sugar basis. For sores in mouth and throat.

The loss of phenol from the lozenges is considerable under all ordinary conditions of storage, and may average 1 mg. per month. The strength is usually under 0.03 g. per lozenge.—C. A. Hill and A. D. Powell, *Quart. J. Pharm.*, 1934, 535.

**[P2] Unguentum Phenolis (B.P.).** *Syn.* UNGUENTUM ACIDI CARBOLICI. Phenol 3% in a basis of white beeswax, lard, hard and soft paraffins. Lard is used owing to the small solubility of phenol in paraffins. For ulcers and parasitic skin diseases.

Water-miscible bases should be used for all ointments, such as ointment of phenol, intended for use as bactericides.—E. Gershenfeld and R. E. Miller, *Amer. J. Pharm.*, 1933, 194.

The loss of phenol from phenol ointment during the preparation of small quantities may be from 3.7 to 5.2% of the phenol added. Ointments prepared in accordance with the *B.P.* and stored in pots at room temperature lose phenol rapidly, and the strength may fall as low as 2% after two years' storage. More rapid loss occurs at higher temperatures. Specimens stored in collapsible tubes show little loss of phenol after ten months' storage.—G. R. Page, *Quart. J. Pharm.*, 1933, 373.

The loss of phenol in preparing about 250 g. of phenol ointment by ordinary methods is approximately 5%. Storage in collapsible tubes reduces the loss of phenol to a negligible amount even after one year. In well-closed containers the loss in nine months may reach about 8%.—H. Brindle, *Pharm. J.*, ii/1940, 20.

**Unguentum Phenolis (U.S.P. XI).** Phenol 2, yellow wax 5, petrolatum 93. The yellow wax and phenol are melted on a water-bath, the petrolatum added and the mixture stirred until it congeals. It is required to contain from 1.8 to 2.2% of  $C_6H_5OH$ .

[P2] **Unguentum Phenolis Compositum (B.P.C.).** Phenol about 18%, with sulphur, olive oil, beeswax and strong ointment of mercuric nitrate.

**BOILS.** Boils of a subacute type may respond favourably to the following ointment: phenol 1%, camphor 3%, salicylic acid 2%, lanoline-Vaseline  $\frac{1}{2}$  oz. A thick layer of the ointment on a piece of lint is laid on the boil and changed as often as required. Soothing, antiseptic, and hastens separation of the slough. —John Fraser, *Practitioner*, i/1936, 359.

#### Vapor Phenolis.

20 drops of liquefied phenol in a pint of water at 60°. Inhaled or as a spray in pertussis and for throat ulcers.

[P1] **Vapor Phenolis Compositus (B.P.C.).** Creosote 1% v/v, oils of eucalyptus and Siberian fir 2% v/v, in liquefied phenol.

#### Smelling Salts, Carbolised.

Phenol 24, ammonium carbonate 16, strong solution of ammonia 44, oil of lavender  $1\frac{1}{2}$ , camphor 3, pine sawdust (sifted) q.s. For coryza, hay fever, influenza, etc.

#### Anti-Catarrhal Salts.

Phenol 1, eucalyptus oil 1, oil of pumilio pine  $\frac{1}{2}$ , strong solution of iodine  $\frac{1}{2}$ , camphor 1, ammoniated alcohol 2, pine sawdust 2 or q.s.

[P1] **Anusant Suppositories (Allen & Hanburys, London)** contain phenol, adrenaline, zinc oxide, benzocaine and Peru balsam in a lanolin base. **Anusant Ointment** contains the first three ingredients in a lanolin base. For hæmorrhoids, etc.

[P2] **Emollientine (Parke, Davis, London).** Ointment containing phenol 4½ gr. and mercuric chloride  $\frac{1}{2}$  gr. per ounce, with lead oxide, zinc sulphocarbonate, etc. Beneficial in eczema, hæmorrhoids, ulcers, etc.

**Inhalone (Parke, Davis, London).** Ointment containing phenol 1½ gr. per oz., menthol and eucalyptol in soft paraffin. Relieves congestion of nasal passages.

**Phenofax (Burroughs Wellcome, London).** Phenol ointment containing 3% of phenol. In pruritus and irritant skin conditions and as a stimulating dressing for small wounds.

**Acidum Phenolsulphonicum.**  $C_6H_4(OH)SO_3H = 174.1$ .

*Syn.* SULPHOCARBOLIC ACID, SOZOLIC ACID.

Prepared by the action of strong sulphuric acid on phenol. The *para*-acid is produced in the warm, the *ortho*-when working in the cold; crystallises with difficulty, dissolves readily in water, alcohol, and glycerin, and is a strong antiseptic and disinfectant.

**Sodii Phenolsulphonas (B.P.C.).** *Syn.* SODII SULPHOCARBOLAS.  $C_6H_4(OH)SO_3ONa \cdot 2H_2O = 232.1$ .

*Dose.*—5 to 15 grains (0.3 to 1 g.).

In white rhombic crystals, slightly efflorescent in dry air.

**Soluble** 1 in 6 of water, 1 in 150 of alcohol 90%, 1 in 5½ of glycerin.

**Uses.** In dilatation of the stomach due to flatulence and fermentation. For flatulence, the dyspepsia of phthisis and in tonsillitis 5 to 10 grains every 2 hours have been given.

**Mist. Sod. Sulphocarb. (N.I.F.).** Sodium phenolsulphonate 5 gr., potassium bicarbonate 10 gr., water to  $\frac{1}{2}$  oz.



**Zinci Phenolsulphonas (B.P.C.).**

*Syn.* ZINCI SULPHOCARBOLAS.  $(C_6H_4(OH)SO_3)_2Zn \cdot 8H_2O = 555.7$ .  
Colourless rectangular crystals. Soluble 1 in 2 of water, 1 in  $2\frac{1}{2}$  of alcohol 90%.

In gonorrhœa and leucorrhœa; 2 or 3 gr. per oz. for injection.  
Also as a nose or throat spray (5 gr. per oz.).

**Tribromophenol.** *Syn.* BROMOL.  $C_6H_2Br_3 \cdot OH = 330.7$ .

*Dose.*  $\frac{1}{2}$  to 2 grains (0.03 to 0.12 g.) in pill.

In silky needles, nearly insoluble in water, soluble 1 in 3 of alcohol 90%, 1 in 1 of ether, 1 in 3 of chloroform and glycerin; also soluble in fats and oils. M.p.  $85^\circ$ . Is used as an intestinal disinfectant and in typhoid, also in minute doses for cholera infantum.

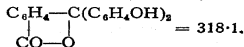
**Bismuthi Tribromphenas (B.P.C., P. Helv. V, P.G. VI).** *Syn. and Prop. Name.* BROMPHENOL BISMUTH, BROMPHENOBIS, BISMUTUM TRIBROMOPHENYLICUM (P. Ital. V), XEROFORM (Heyden, Dresden; Braun, London). No formula is given in B.P.C. P. Helv. V gives  $(C_6H_2Br_3O)Bi(OH)_2Bi_2O_3$ .

*Dose.*—5 to 15 grains (0.3 to 1 g.).

A yellowish insoluble powder, with faint odour and taste, containing 40.5 to 49.5% of Bi. An intestinal antiseptic, e.g., for cholera.

**PHENOLPHTHALEINUM**

*B.P., U.S.P. XI, Fr. Cx., etc.*



*Syn. and Prop. Name.* DIHYDROXYPHTHALOPHENONE, LAXOIN (Oppenheimer, London).

*Dose.*—1 to 5 grains (0.06 to 0.3 g.). Larger doses are used.  
*U.S.P. XI* average dose 1 grain.

A white crystalline powder, made by interaction of phenol and phthalic anhydride. M.p. (B.P. Add. I) not below  $258^\circ$ ; commercial samples may melt at temperatures up to  $260^\circ$ .

**Soluble** 1 in 10 of alcohol 90%, also soluble in ether; almost insoluble in water.

**Uses.** A mild, tasteless purgative, of value in habitual constipation, and ordinarily non-toxic even in large doses. It acts in about six hours and is best given at bed-time; its action continues with diminishing intensity for two or three days. Usually a dose of  $\frac{1}{2}$  to 3 gr. is sufficient, but bed-ridden patients may require up to 8 gr. It is more active than cascara and less griping, and is said to be the ideal purgative in intestinal toxæmia. In susceptible subjects it occasionally gives rise to an urticarial rash, and cases are on record in which the absorbed drug has produced backache, albuminuria and free hæmoglobin in the urine.

An investigation into the effect of phenolphthalein upon patients and normal individuals showed that medicinal doses do not produce albuminuria, and even in those patients who already had albuminuria the administration did not result in any increase in the proportion of albumen in the urine.—B. Fantus and J. M. Dyniewicz, *J. Amer. med. Ass.*, i/1937, 439.

In case of an overdosage there should be administered at the earliest possible moment at least twenty-five times the amount of activated charcoal diffused through water—this may be given in divided doses if necessary. If the patient

has taken a very large quantity of phenolphthalein it might possibly be advisable to follow this by a tablespoonful of castor oil, which is preferable to magnesium sulphate.—B. Fantus and J. M. Dyniewicz, *J. Amer. med. Ass.*, 1/1938, 1656.

**Tabellæ Phenolphthaleini (B.P.C.)** contain 2 gr. (0.12 g.) in chocolate basis.

[P1] **Tabellæ Phenolphthaleini Compositæ (B.P.C.)**.

*Dose.*—1 to 3 tablets.

Phenolphthalein 1 gr., strychnine hydrochloride  $\frac{1}{100}$  gr., dry extract of belladonna  $\frac{1}{100}$  gr. A useful combination.

**Isolax (Richter, London)**. Diphenolisatin in tablets containing 0.005 g.

*Dose.*—1 or 2 tablets nightly. Aperient.

[P1-S1] **Phenalos (Sharp & Dohme, London)**. Tablets contain phenolphthalein  $\frac{1}{2}$  gr., aloin  $\frac{1}{2}$  gr., strychnine nitrate  $\frac{1}{10}$  gr., extract of belladonna  $\frac{1}{2}$  gr., powdered ipecac.  $\frac{1}{10}$  gr.

**Purgen (Kirby, London)**. Tablets containing phenolphthalein. Supplied as infant ( $\frac{1}{2}$  gr.), adult ( $1\frac{1}{2}$  gr.) and strong ( $7\frac{1}{2}$  gr.).

**Fluoresceinum Solubile (B.P., U.S.P. XI)**. *Syn.* SODIUM FLUORESCIN, URANIN, OBITURIN.  $C_{20}H_{10}O_5Na_2 = 376.1$ .

Red crystalline powder, forming a red solution with intense greenish-yellow fluorescence which disappears on acidifying.

**Soluble** 1 in 1 of water, 1 in 5 of alcohol 90%.

**Uses.** The solution is used for detecting corneal lesions, *e.g.*, when due to a minute foreign particle in the eye. Portions of the cornea not covered by epithelium are stained green. Has been employed by injection as a proof of death. If life is extinct there is no reaction; if death is only apparent, the integument and the eyes turn green in a few minutes. A slightly alkaline (not neutral) solution of soluble fluorescein sprayed or painted widely over the surface of the growth, followed by radium or X-ray irradiation of moderate penetration, has been employed in the treatment of cancer. (*For formulæ of paint, injections, and capsules see Vol. I, 21st Edn., pp. 755-6.*)

**Guttæ Fluoresceinæ (B.P.C.)**. *Syn.* LIQUOR FLUORESCINÆ.

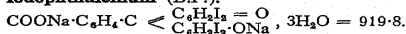
Soluble fluoresceine 2% w/v.

**Eosin (Colour Index No. 768)** is the sodium or potassium salt of tetrabromofluorescein. A reddish-brown powder soluble in water giving a red solution with green fluorescence. Ethyl eosin or spirit-soluble eosin (Colour Index No. 770) is the potassium salt of dibromo-dinitrofluorescein.

**Fluorescein**. *Syn.* TETRAOXYPHTHALOPHENONE ANHYDRIDE, RESORCIN-PHTHALEIN ANHYDRIDE.  $C_{20}H_{12}O_5 = 332.1$ .

In yellowish-red powder, sparingly soluble in water, more so in presence of an alkali, *e.g.* sodium hydroxide, forming soluble fluorescein showing a green fluorescence.

**Iodophthaleinum (B.P.)**.



*Syn. and Prop. Names.* IODOPHTHALEINUM SOLUBILE (U.S.P. XI), SODIUM TETRAIODOPHTHALEIN, IODO-RAY (Martindale, London), IOD-TETRAGNOST (Merck, Darmstadt; Martindale, London), OPACIN (Pharmaceutical Specialities (May & Baker) Ltd., London), STIPOLAC (Burroughs Wellcome, London), T.I.P. (Boots, Nottingham).

**Dose.**— $\frac{1}{4}$  to  $\frac{1}{2}$  grain per pound body weight up to 75 grains (0.04 to 0.06 g. per kilogramme body weight up to 5 grammes). By intravenous injection, up to 45 grains (3 g.). *U.S.P. XI* average doses, oral 8 grains, intravenous 5 grains, per 10 kg. body weight.

A blue-coloured powder, somewhat hygroscopic, with a saline astringent taste. An aqueous solution may throw out on standing, owing to absorption of carbon dioxide and deposition of the acidic body. It yields not less than 85% of the cream-coloured tetraiodophenolphthalein on precipitation with hydrochloric acid, the separated precipitate containing 61 to 62% of I.

**Soluble** 1 in 7 of water; slightly soluble in alcohol 90%.

**Uses.** It has been advocated as the most suitable of numerous chemicals which, following intravenous or oral administration, are excreted by the liver into the gall-bladder, rendering it opaque to X-rays (cholecystography). (*See Vol. II.*)

#### Sodium Tetrabromphenolphthalein.



**Dose.**—The dose *per os* is from 4 to 7 g., according to weight of the patient, the average dose being about 5 g.

A pale mauve powder readily soluble in distilled water. Both the powder and solutions should be preserved from the action of the air, as carbon dioxide is slowly absorbed. It has been used for cholecystography, but iodophthalein is now preferred.

#### Phenol-Rubrum (B.P.C., U.S.P. XI).

*Syn.* PHENOL RED, PHENOLSULPHONPHTHALEIN (*Fr. Cx.*).

**Dose.**—(By injection)  $\frac{1}{10}$  grain (0.006 g.). A bright to dark red crystalline powder slightly soluble in water. Employed as a test for permeability of the kidney. (*See Vol. II.*)

## PHOSPHORUS

*B.P.C., Fr. Cx., P. Helv. V, P. Dan.*

P = 31.02.

[P1] “Phosphorus, yellow.”

**Dose.**— $\frac{1}{100}$  to  $\frac{1}{5}$  grain (0.0006 to 0.0025 g.). *Fr. Cx.* has max. single dose  $\frac{1}{4}$  grain; max. during 24 hours  $\frac{1}{2}$  grain.

A poisonous, non-metallic element melting at 44° and igniting at a slightly greater heat, forming white fumes of phosphorus pentoxide.

Phosphorus necrosis, in consequence of the introduction of the sulphide method of making matches, has entirely disappeared.—Sir Thos. Oliver, *Brit. med. J.*, ii/1925, 530.

**Soluble** about 1 in 320 of absolute alcohol, about 1 in 80 of ether, about 1 in 25 of chloroform, about 1 in 100 each of oleic

acid, suet and oils of almond, olive, castor and theobroma, 2 in 1 of carbon disulphide, almost insoluble in water; combines chemically with oils of turpentine and peppermint, forming non-luminous and comparatively non-poisonous liquids.

**Antidotes.** Wash out stomach thoroughly with 1% potassium permanganate solution, using stomach tube. If this is not available give 5 gr. of copper sulphate in water, repeating the dose, first as emetic then as antidote; or use stomach tube with dilute solution of copper sulphate, 15 gr. to 2 gallons of water. Give medicinal charcoal with  $\frac{1}{2}$  oz. of magnesium sulphate, repeating the charcoal frequently. Alkaline drinks and dextrose, but *not* oils, fats or eggs.

**BURNS.** The best immediate treatment is intermittent immersion of the burnt part in a warm 5% solution of sodium bicarbonate which neutralises the phosphoric acid evolved. The part must be taken out from time to time to allow complete combustion of adherent particles of phosphorus, and treatment must be continued until  $P_2O_5$  can no longer be detected by emission of white vapour or garlicky smell and there is no luminosity in a darkened room.—W. Starz, *Munch. med. Wschr.*, 1/1936, 47.

**Uses.** Phosphorus has been employed as a nerve stimulant in various affections of the central nervous system and in osteomalacia and rickets, but is now rarely used in the elemental state in medicine. It enters the blood as phosphorus, and acts as such, not as phosphoric acid.

*N.B.—Preparations should be recently made and kept from light.*

[P1] **Elixir Phosphori.**

Add compound solution of phosphorus 1 to glycerin 4.

*Dose.*—15 to 60 minims (1 to 4 ml.) in water. Contains  $\frac{5}{16}$  gr. in 1 dr. A palatable, well-tolerated "fluid" form of phosphorus.

[P1] **Liquor Phosphori Compositus (B.P.C.).** *Syn.* TINCTURA PHOSPHORI COMPOSITA.

*Dose.*—3 to 12 minims (0.2 to 0.8 ml.), on sugar.

Phosphorus 0.2% w/v in chloroform and dehydrated alcohol. 12 minims contains about  $\frac{3}{16}$  gr. of phosphorus.

[P1] **Oleum Phosphoratum (B.P.C.).**

*Dose.*—1 to 5 minims (0.06 to 0.3 ml.), on sugar or in perles.

Contains 1% w/w of phosphorus in almond oil flavoured with oil of lemon. *P. Ital.* V is 0.1% in olive oil. *P. Belg.* IV contains no oil of lemon. *P. Helv.* V and [P1] **Phosphorus solutus** (*P.G.* VI) are 0.5% w/w in liquid paraffin with ether 2½% w/w. *P. Svec.* X has 1% in liquid paraffin with 5% of ether.

**ORIENTAL SORE.** Best results in old intractable cases with extensive ulceration, the oil being dabbed on after removing the scab, every other day. When ulcerative process not well developed and lesion is nodular, inject 3 to 5 m. hypodermically round or into nodule once or twice weekly; injection practically painless. No general reaction and local reaction slight, but signs of acute inflammation occasionally develop. The delayed action of phosphorus on the liver should be kept in mind.—A. Castellani, *J. trop. Med. (Hyg.)*, 1925, 377. See also *ibid.*, 1923, 194.

[P1] **Pilulæ Phosphori (B.P.C.).**

*Dose.*—1 to 4 pills. Contain  $\frac{1}{100}$  gr. of phosphorus.

Compound phosphorus pills are sometimes used containing  $\frac{1}{32}$ ,  $\frac{1}{16}$  or  $\frac{1}{80}$  gr., with strychnine  $\frac{1}{16}$  gr., or extract of nux vomica  $\frac{1}{4}$  gr. Also with extract of damiana or zinc valerianate and in combination with reduced iron and quinine sulphate.

**Zinci Phosphidum** (B.P.C., Fr. Cx.).  $\text{Zn}_3\text{P}_2 = 258.2$ .

*Dose.*— $\frac{1}{2}$  to  $\frac{1}{4}$  grain (0.003 to 0.016 g.) in pill. Fr. Cx. has max. single dose  $\frac{1}{4}$  grain; max. during 24 hours  $\frac{1}{2}$  grain approx.

A grey powder with slight phosphorus odour. Exerts the same action as phosphorus and can be administered in pills, but is incompatible with acid vegetable extracts (e.g., extract of gentian) owing to liberation of hydrogen phosphide.

## PHYSOSTIGMA

B.P.C.

*Syn.* PHYSOSTIGMATIS SEMINA, CALABAR BEAN (Fr. Cx.), ORDEAL BEANS.

[P1] "*Alkaloids, the following; their salts, simple or complex:—Calabar bean, alkaloids of.*"

[S1] "*Alkaloids, the following; their salts, simple or complex:—Calabar bean, alkaloids of.*"

[S6] "*Alkaloids—calabar bean, alkaloids of—specify proportion as the proportion of any one alkaloid of calabar bean that the preparation would be calculated to contain on the assumption that all the alkaloids of calabar bean in the preparation were that alkaloid.*"

*Dose.*—1 to 4 grains.

The ripe seeds of *Physostigma venenosum* (Leguminosæ), from West Africa. The poisonous properties are due chiefly to the presence, in the cotyledons only, of physostigmine (up to about 0.25%).

**Antidotes.** Empty stomach by emetic or by stomach tube, using 60 gr. of potassium permanganate in 2 gallons of water. Medicinal charcoal or Lugol's solution has been recommended. Atropine sulphate,  $\frac{1}{30}$  gr. hypodermically, is the physiological antidote. Give  $\frac{1}{4}$  oz. of brandy or  $\frac{1}{2}$  dr. of aromatic spirit of ammonia, in water freely. Strychnine,  $\frac{1}{2}$  gr. hypodermically. Artificial respiration may be necessary.

Pulmonary edema, with death in 15 minutes, following injection of  $\frac{1}{30}$  gr. of eserine in a young woman. Atropine injection did not affect the result.—W. E. Cooke, *Brit. med. J.*, i/1937, 1052.

**Uses.** The properties of the calabar bean are virtually those of the alkaloid physostigmine (*vide infra*), and it is used only as the source of this alkaloid and its salts.

[P1-S1] **Physostigmina.** *Syn.* ESERINE (Fr. Cx.).

$\text{C}_{15}\text{H}_{21}\text{N}_3\text{O}_2 = 275.2$ .

*Dose.*— $\frac{1}{100}$  to  $\frac{1}{50}$  grain (0.0006 to 0.0013 g.).

In colourless crystals, slightly soluble in water, freely in alcohol and ether, soluble 1 in 180 of soft paraffin, also soluble in other fixed oils. Is used for the preparation of ointments and solutions in oil for use as miotics. For corneal ulcers, [P1-S1] solution of 2 gr. per oz. may be dropped into the eye; also in mydriasis and glaucoma.

**Uses.** The physiological actions of physostigmine may be divided into four main groups:—(1) INCREASED IRRITABILITY OF THE AUTONOMIC NERVES, resulting in slowing of the pulse by

stimulation of the vagus and contraction of the pupil by stimulation of the oculomotor nerve. By virtue of its miotic action, it is widely used in glaucoma to decrease intra-ocular tension, to prevent and treat prolapse of the iris in peripheral corneal ulcer or wound, and to counteract the effect of atropine or homatropine. (2) **STIMULATION OF UNSTRIPED MUSCLE**, especially that of the intestine. As a stimulant to peristalsis it is useful in chronic constipation, post-operative intestinal atony, post-operative distension and flatulent colic. It may also be employed to increase tonicity in routine X-ray examination of the stomach when it is dilated and borders are indistinct. (3) **DEPRESSION OF THE CENTRAL NERVOUS SYSTEM**, resulting in diminution of the reflex activities; and as a sedative of the spinal cord it has been used in tetanus. (4) **TWITCHING OF THE VOLUNTARY MUSCLES**; while small doses lower the threshold to stimulation of striped muscle, somewhat larger doses produce fibrillary twitchings. This effect has been beneficially employed in the treatment of myasthenia gravis. The unpleasant symptoms, such as abdominal discomfort and nausea, may be prevented by the previous administration of atropine or tincture of belladonna.

[P1-81] **Guttæ Physostigminæ Oleosæ (B.P.C.)**. Physostigmine (base)  $\frac{1}{2}\%$  in castor oil. Keeps well for ophthalmic use.

Severe frontal headache in young persons due to increased intra-ocular tension, cured by eserine instillations *t.d.s.*—R. L. Raymond, *Brit. med. J.*, i/1934, 103.

[P1-81] **Unguentum Physostigminæ**. *Syn.* UNGUENTUM ESERINÆ (R.L.O.H.). Physostigmine 1 or 2 gr. dissolved in minimum quantity of chloroform and mixed with yellow soft paraffin (at 61°) to 1 oz.

[P1-81] **Physostigminæ Salicylas (B.P., U.S.P. XI, P. Helv. V, etc.)**. *Syn.* ESERINE SALICYLATE (*Fr. Cx.*).

$C_{15}H_{21}O_5N_3, C_7H_5O_3 = 413.2$ .

*Dose.*— $\frac{1}{100}$  to  $\frac{3}{50}$  grain (0.0006 to 0.0012 g.). Doses of up to  $\frac{1}{50}$  grain (0.003 g.) are sometimes administered. *U.S.P. XI* average dose  $\frac{3}{50}$  grain.

In needle-shaped or columnar crystals. Soluble about 1 in 100 of water and 1 in 12 of alcohol 90%. Solutions are less liable to turn pink than those of the sulphate.

To open the bowels in acute abdominal conditions,  $\frac{1}{100}$  grain hypodermically until 6 doses have been given (4-hourly). This dose is safe—higher dose may act too severely and necessitate bismuth and opium to check the resulting diarrhoea. If no action, give a turpentine enema the following day.

**MYASTHENIA GRAVIS.** Physostigmine, being a partial antagonist to curare, was tried in the hope that it would counteract the effect of the unknown substance which might be exerting the curare-like effect on the myoneural junctions. *Hypodermic injections* of physostigmine salicylate were found to have a striking though temporary effect. Injections of  $\frac{3}{50}$  gr. once daily were of value, but effect wore off in 2 to 4 hours. Greater improvement with  $\frac{3}{50}$  gr., lasting 4 to 5 hours.—M. B. Walker, *Lancet*, i/1934, 1200.

[P1-81] **Guttæ Physostigminæ (B.P.C.)**. *Syn.* GUTTÆ ESERINÆ.

Physostigmine salicylate 1% *w/v*, with boric acid, in distilled water. *N.I.F.* has  $\frac{1}{2}$  gr. in water to 2 dr.

[P1-S1] **Lamella Physostigminæ (B.P.).** *Syn.* LAMELLA ESERINÆ. Each contains  $\frac{1}{1000}$  grain (0.00065 g.) of physostigmine salicylate.

[P1-S1] **Oculentum Physostigminæ (B.P.).** *Syn.* OCULENTUM ESERINÆ.

Contains 0.125% of physostigmine salicylate.

[P1-S1] **Physostigminæ Sulphas (B.P.C., P.G. VI, P. Ned. V, F.E. VIII).** *Syn.* ESERINE SULPHATE.

$(C_{15}H_{21}O_2N_3)_2 \cdot H_2SO_4 = 648.5$ .

*Dose.*— $\frac{1}{100}$  to  $\frac{1}{30}$  grain (0.0006 to 0.0012 g.). (B.P. '14,  $\frac{1}{8}$  to  $\frac{1}{2}$  grain.)

In yellowish, granular, deliquescent crystals, soluble about 4 in 1 of water and 2.5 in 1 of alcohol 90%. Solution becomes pink on exposure, but does not lose much in efficacy.

In doses of  $\frac{1}{100}$  grain (0.0006 g.) of value in tympanites as occurring in typhoid fever.

[P1-S1] **Guttæ Physostigminæ (R.L.O.H.).**  $\frac{1}{2}$ , 1, 2 or 4 gr. to 1 oz. *St. T. H.*, 0.125, 0.25, 0.5 or 1%. *St. M. H.*, 0.25, 0.5 or 1%.

In glaucoma the 0.5 to 1% drops are suited for prolonged use.

The 1% solution instilled 2 or 3 times a day is of value. It contracts the pupils and greatly improves vision.—*J. trop. Med. (Hyg.)*, 1926, 303.

[P1-S1] **Mistura Physostigminæ Laxativa (B.V.H.).** Physostigmine sulphate  $\frac{1}{10}$  gr., liquid extract of cascara sagrada 1 dr., ammoniated tincture of podophyllum 15 m., liquid extract of liquorice 15 m., syrup 15 m., compound decoction of aloes to 1 oz.

**Geneserine (Amido Laboratories, Paris; Wilcox, JozEAU, London).** The amino oxide of eserine. Supplied in granules containing 0.5 mg. (*dose*—from 6 to 10 granules daily in three doses); in 1 in 1000 solution (*dose*—20 drops = 1 mg. of Geneserine, three times daily); and in ampoules containing 2 mg. for subcutaneous injection. Therapeutic action and indications similar to those for eserine but is much less toxic and better tolerated.

**Prostigmin (Roche Products, Welwyn Garden City).** Dimethyl-carbamic ester of 3-hydroxyphenyltrimethylammonium-methylsulphate. A synthetic peristaltic stimulant allied to physostigmine, but stable in solution and safer in use. It is given by subcutaneous, intramuscular or intravenous injection in post-operative intestinal paresis, severe constipation, retention of urine, myasthenia gravis, etc. Ampoules of 1 ml. contain 0.5 mg. of active substance. Also supplied in concentrated solution, 1 ml. containing 2.5 mg., and in tablets each containing 15 mg.

*Severe poisoning* of a research worker following experimental ingestion of 45 mg. Recovery after injection of atropine sulphate,  $\frac{1}{30}$  grain intramuscularly. If Prostigmin is needed in myasthenia gravis it should be given parenterally so that dosage can be controlled. If the latter is impossible it seems wisest to rely on other therapeutic measures until more is known concerning oral Prostigmin.—L. S. Goodman and W. J. Bruckner, *J. Amer. med. Ass.*, 1/1937, 965.

**MYASTHENIA GRAVIS.** Beneficial results in every one of 7 cases which, though lasting for only a few hours, surpassed anything experienced with other methods of treatment. The injection was given subcutaneously—Prostigmin 2 ml. with atropine  $\frac{1}{30}$  gr. Unpleasant symptoms only of a mild nature.—L. P. E. Laurent, *Brit. med. J.*, 1/1935, 465.

Seven patients treated with Prostigmin, usually 5 ml., in conjunction with atropine sulphate  $\frac{1}{30}$  gr. In each case improvement set in within 5 minutes of the injection, passing off completely in 8 hours.—E. A. B. Pritchard, *Lancet*, 1/1935, 432.

From the practical point of view it is now possible to abolish the more serious symptoms and to keep the patients in a tolerable state of health by means of ephedrine and eserine or Prostigmin.—A. M. Cooke and R. Passmore, *Quart. J. Med.*, Jan., 1936, 28.

From 25 to 30 mg. of Prostigmin *per os* gives a result comparable in intensity and duration with an injection of 0.5 mg.—L. P. E. Laurent and M. B. Walker, *Lancet*, i/1936, 1457.

The oral administration of Prostigmin seems at present to be the most valuable therapeutic agent in the treatment of myasthenia gravis, although some patients are not completely relieved of symptoms by its use.—A. M. Harvey and M. R. Whitehill, *J. Amer. med. Ass.*, i/1937, 1329.

It is possible that Prostigmin may find its widest usefulness as a test to differentiate myasthenia gravis from other causes of muscular weakness, since it relieves no other condition. As a test dose from 1.5 to 2 mg. hypodermically is used with atropine sulphate  $\frac{1}{100}$  grain. Children tolerate about half the adult dose.—G. D. Gammon and H. Schlie, *J. Amer. med. Ass.*, ii/1937, 413.

Oral administration of Prostigmin may be safely used in the treatment of patients with myasthenia gravis in daily doses of from 3 to 12 tablets of 15 mg. each. When ingestion of the drug is carefully spaced (usually three- to four-hourly intervals between doses) patients maintain a reasonable degree of muscular efficiency. No ill effects were noted in 18 patients treated for one to fourteen months.—H. R. Viets *et al.*, *J. Amer. med. Ass.*, ii/1937, 1956.

The results of the treatment of 44 patients with myasthenia gravis over a period of 2½ years indicate that *Prostigmin bromide*, taken by mouth and supplemented by ephedrine sulphate, potassium chloride and guanidine, is the most efficient form of treatment now available. Of the 44 patients, 5 have died and 7 have shown full remissions so that Prostigmin is no longer required. Prostigmin bromide may be given in daily doses of from 20 to 25 pills of 15 mg. each. More important than the size of the dose is the spacing of the drug through the 24-hour period, and regulation of the dosage to ensure max. effects being produced without tolerance or disagreeable effects may take weeks or even months.—H. R. Viets and R. S. Schwab, *J. Amer. med. Ass.*, ii/1939, 559.

Recently it has been observed that a combination of guanidine hydrochloride (0.0125 g.), potassium chloride (5 to 10 g.), and Prostigmin (0.015 g.), taken with meals, gives a sustained effect for 3 or 4 hours, though such a combination of anti-myasthenia drugs is only necessary in the most desperate cases.—J. H. Talbott and R. S. Schwab, *New Engl. J. Med.*, i/1940, 585.

PARALYTIC ILEUS cured by 5 ml. of Prostigmin subcutaneously after almost every known remedy (except acetylcholine) had failed.—W. E. David, *Lancet*, i/1935, 1100.

Prevention of post-operative ileus with Prostigmin.—W. R. Lewis and E. L. Axelman, *Amer. J. Surg.*, i/1936, 308.

After enemas of all kinds, Pituitrin and acetylcholine had all failed, a case was successfully treated by two injections subcutaneously of 5 ml. of Prostigmin, one given at noon and one at 7 p.m.—R. C. Begg, *Brit. med. J.*, ii/1937, 581.

As a result of its use in a series of 175 cases it was concluded that Prostigmin is a satisfactory agent for the prevention or treatment of distension and paralytic ileus. It has a wide margin of safety and injections may be made at two-hourly intervals.—J. R. Harger and J. L. Wilkey, *J. Amer. med. Ass.*, i/1938, 1165.

The presence of intestinal flatus often results in poor definition in X-ray films of the abdomen. A preliminary injection of Prostigmin 2 ml. (1 mg.) the night before examination and a similar dose the following morning one hour before taking the X-ray photograph leads to the production of a more satisfactory film.—M. J. Farrell, *New Engl. J. Med.*, ii/1938, 270.

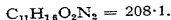
POST-OPERATIVE DISTENSION. Prostigmin is a valuable prophylactic for preventing post-operative distension and gas pains. With inhalation anaesthetics the first injection is given 3 to 4 hours after operation, followed by a second injection 4 hours later; four injections are given at intervals of 4 hours the first day after operation, and the last dose followed immediately by a low soapuds enema. With this method the prophylactic peristalsis is established within 24 hours of the operation, whereas prior to its use in abdominal cases peristalsis was not established for 48 and in some cases 72 hours. There is no systemic



or local reaction.—W. R. Levis and E. L. Axelman, per *J. Amer. med. Ass.*, ii/1936, 310.

**Esmodil** (*Bayer Products, London*). An 0.3% isotonic aqueous solution of trimethyl-methoxy-propanyl-ammonium bromide, for stimulation of the parasympathetic nerves. *Dose*.—1 ml. intramuscularly or subcutaneously, repeating  $\frac{1}{2}$  ml. in 2 to 3 hours if necessary.

## PILOCARPINA



[P1] "*Alkaloids, the following; their salts, simple or complex:—Jaborandi, alkaloids of.*"

[S1] "*Alkaloids, the following; their salts, simple or complex:—Jaborandi, alkaloids of, except substances containing less than 0.5% of the alkaloids of jaborandi.*"

[S3] "*Alkaloids—Jaborandi, alkaloids of—in substances containing less than 0.025% of the alkaloids of jaborandi.*"

*Dose*.—*Fr. Cx.* has max. single dose  $\frac{1}{2}$  grain (0.02 g.); max. in 24 hours  $\frac{3}{4}$  grain (0.05 g.).

An alkaloid obtained (0.5%) from *Pilocarpus microphyllus* (Maranham Jaborandi) and other varieties.

Easily **soluble** in water. Soluble in alcohol, ether, chloroform and benzene.

**Antidotes.** Empty stomach by emetic or stomach tube. Give potassium permanganate, 10 gr. in 1 pint of water, by stomach tube, and repeat the dose if necessary. Atropine,  $\frac{1}{100}$  gr., hypodermically, or tincture of belladonna by mouth; this is the specific antidote. Stimulants, *e.g.*, brandy,  $\frac{1}{2}$  oz., or aromatic spirit of ammonia,  $\frac{1}{2}$  dr., in water freely.

**Uses.** A powerful sudorific and sialogogue when administered internally. Large doses have an emetic action. The sweating and salivation commence about 10 minutes after taking a dose and persist for 2 to 5 hours. Hypodermically it acts in 3 to 5 minutes. It has been given in dropsy of renal origin, but must not be given in cardiac dropsy owing to its depressant action on the heart and it should be avoided in pulmonary disease, since the increase of mucus and the action on the circulation may result in pulmonary oedema. It increases the flow of biliary mucus, and has been given to assist the passage of gall-stones. In puerperal eclampsia and uræmic convulsions, it has been given to induce diaphoresis, preferably in conjunction with the external application of heat. In tinnitus aurium (acute labyrinthine) hypodermic injections with gradually increasing dosage are of value in suitable cases. For hiccough small doses every 2 or 3 hours are of value. Salts of pilocarpine have been employed as antidotes to belladonna poisoning, but they do not prevent death from large doses since they only act peripherally.  $\frac{1}{10}$  gr. doses have been given to counteract the effects of hyoscine used in the treatment of morphine addiction by sudden withdrawal and to relieve the dryness of the

mouth associated with the atropine or belladonna treatment of parkinsonism. Externally preparations of jaborandi and pilocarpine are used to stimulate growth of hair in alopecia. The 2% solution is used as a miotic; it is less irritating than physostigmine, but its action is weaker and more evanescent, miosis lasting for 18 to 24 hours.

**POST-OPERATIVE RETENTION OF URINE.** Pilocarpine *intrav.*  $\frac{1}{2}$  grain, or *per rectum*  $\frac{1}{2}$  grain, often successful where hexamine fails.—*per Med. Annu.*, 1931, 10. Brief experience favourable.—A. R. Short, *ibid.*

[P1-81] **Pilocarpinæ Hydrobromidum.** *Dose.*— $\frac{1}{10}$  to  $\frac{1}{2}$  grain (0.003 to 0.012 g.). White crystals soluble in water. Used similarly to the nitrate.

### **Syrupus Potassii Bromidi et Pilocarpinæ (B.P.C.).**

*Dose.*—1 to 2 drachms (4 to 8 ml.).

1 drachm contains potassium bromide about  $5\frac{1}{2}$  gr. and pilocarpine hydrobromide  $\frac{3}{16}$  gr. in an orange-flavoured medium.

**Bromocarpine** (prepared in England by *Roberts & Co., London*) is a similar product, stated to have the composition potassium bromide 10, pilocarpine hydrobromide 0.005, orange syrup and glycerin *q.s.* to 100, *by weight.* *Dose.*—For children 3 to 7 years of age 1 to 3 drachms daily; 7 to 15 years 1 to 6 drachms daily; adults  $\frac{1}{2}$  to 1 ounce daily, *all in divided doses.*

[P1-81] **Pilocarpinæ Hydrochloridum (B.P.C., P.G. VI, Fr. Cx., P. Ned. V, P. Helv. V, etc.).**  $C_{11}H_{15}O_2N_2.HCl = 244.6$ .

*Dose.*— $\frac{1}{10}$  to  $\frac{1}{2}$  grain (0.003 to 0.012 g.) by mouth or hypodermically.

In minute, granular, snow-white crystals, slightly deliquescent and very soluble in water. Used similarly to the nitrate.

[P1-81] **Pilocarpinæ Nitrates (B.P., U.S.P. XI, Fr. Cx., F.E. VIII, P. Ned. V).**  $C_{11}H_{15}O_2N_2.HNO_3 = 271.2$ .

*Dose.*— $\frac{1}{10}$  to  $\frac{1}{2}$  grain (0.003 to 0.012 g.). *Fr. Cx.* has max. single dose  $\frac{1}{2}$  grain; max. in 24 hours  $\frac{3}{4}$  grain approx. *U.S.P. XI* average dose  $\frac{1}{12}$  grain.

In minute, white, granular, snow-like crystals, but may be obtained in large, white, prismatic crystals. Soluble 1 in 8.2 of water, but very slightly in cold alcohol.

[P1] **Guttæ Pilocarpinæ (B.P.C.).** 0.5% of pilocarpine nitrate. Used to contract the pupil of the eye.

[P1-81] **Lamella Pilocarpinæ.**  $\frac{3}{16}$  gr. in a gelatin base.

[P1-81] **Lotio Pilocarpinæ.** For the hair.

Pilocarpine nitrate 2 gr., quinine hydrochloride 8 gr., glycerin 2 dr., rose water 6 dr. [P1-81] Tincture of cantharidin 1 dr. may be usefully combined with above quantities.

Applied locally to the scalp, pilocarpine seems to have an action in promoting the growth of hair in alopecia or dandruff. Used also in [P1-81] **Ointment**, 4 gr. to the ounce of a mixture of wool fat and soft paraffin ointment.

[P1-81] **Jaborandi (B.P.C., Fr. Cx., P. Helv. V).** *Syn.* PILOCARPUS.

The dried leaflets of *Pilocarpus microphyllus* (Rutaceæ), containing the alkaloids, pilocarpine (up to about 0.5%), isopilocarpine and pilosine. *P. Helv. V* describes the dried leaves of *P. Jaborandi*, and *Fr. Cx.* those of *P. microphyllus*, *P. Jaborandi* and *P. pennatifolius*.

[P1-81] **Extractum Jaborandi Liquidum (B.P.C.).** 1 in 1.

[P1] **Tinctura Jaborandi (B.P.C.).**

*Dose.*—10 to 30 minims (0·6 to 2 ml.). Liquid extract of jaborandi 1, alcohol 45% to 5.

## PILULÆ

**Excipients.** The chief consideration in the preparation of pill masses is the choice of excipient. The following scheme for their preparation is of almost general application.

- (a) When binding material such as gum, fibre, or soft or dry aqueous extracts is present, the ingredients should be massed with syrup of liquid glucose.
- (b) When no binding material is present, as in the case of camphor, sulphur, thymol, resins, reduced iron and crystalline substances such as ferrous sulphate, 5% of compound powder of acacia should be added and the ingredients massed with syrup of liquid glucose. In certain cases it is advisable to substitute liquid glucose for the syrup to give greater cohesiveness.
- (c) Volatile oils and similar substances should be absorbed in powdered curd soap and the mass stiffened with powdered liquorice.
- (d) Oxidising substances such as potassium permanganate should be made into a paste with the minimum amount of wool fat, and the mass stiffened with kaolin or diatomite.

**Coatings.** The practice in vogue in most pharmacies of invariably coating pills, unless otherwise ordered, is advantageous from every point of view. Coated pills are tasteless and elegant in appearance, they are less liable to deteriorate on keeping and are usually more acceptable to the patient than uncoated pills. The following coatings are in general use:—

**VARNISH COATING.** A solution of sandarac in alcohol (95%) 1 in 2 or, for quicker drying, equal volumes of alcohol (95%) and ether. This is the usual form of coating used on the dispensing counter. About 5 to 8 drops of the solution suffice to coat one dozen 5-grain pills.

**SILVER LEAF COATING.** About two leaves are sufficient for twelve 5-grain pills. The pills should be made tacky with dilute mucilage of acacia and then rotated with the silver leaf in a warm, dry, porcelain pot. Silver coating should not be used for pills containing substances liable to affect it, such as sulphides, unless they are previously varnished.

**SUGAR COATING.** This is effected by placing the pills in a hemispherical metallic pan, kept warm while making revolutions, and they are alternately moistened with syrup and dusted with finely-powdered sugar until dry and uniformly covered.

**PEARL COATING.** The pills are first covered with a mucilage of tragacanth (4 grains to 1 fluid ounce with  $\frac{1}{2}$  drachm of syrup); they are then coated by rotating in a pot with French chalk. The operation is repeated several times until a suitable coating has been formed.

**GELATIN COATING.** The pills are held on needles or by suction in a frame, dipped in a solution of 1 part of gelatin in 4 parts of water, and dried. Gelatin coating is very satisfactory.

**Enteric Coatings.** These are coatings designed to render the pills insoluble in the stomach but soluble in the intestines (*see also* glutoid capsules, p. 543). Many substances are used for this purpose, but none of them is perfectly satisfactory. The following are in general use:—

**GLUTOID COATING OR FORMALDEHYDE-GELATIN.** The pills are gelatin-coated in the usual manner, then immersed for 15 minutes in a 2% solution of formaldehyde and dried.

The longer gelatin-coated pills or capsules are immersed in the formaldehyde solution the sooner they disintegrate in an alkaline pancreatic mixture.—H. N. Dale, *Pharm. J.*, ii/1932, 494.

**STEARIC ACID.** The pills are rotated in melted stearic acid and caused to roll out on a large sheet of paper so that the coating dries evenly. When the pill mass is of a non-greasy character it is advisable to moisten the pills with a solution of white wax in ether, allowing the latter to evaporate. Unless this is done the coating tends to crack readily and peel off.

**Stearettes** (*Martindale, London*) are tablets made with a coating containing stearic acid with other ingredients to prevent cracking.

**SALOL COATING.** This is applied in the same manner as stearic acid. Non-greasy pill masses should be similarly waxed before coating, otherwise the salol will not adhere.

**KERATIN COATING.** The pills are moistened by rotation in a pot with a 10% solution of keratin in equal parts of alcohol and strong solution of ammonia, and then shaken out on an oiled tile to dry. The operation is repeated several times and three or four coatings applied.

A solution containing 10% w/v each of cetyl alcohol and mastic in acetone is advocated as an enteric coating.—L. M. Mills, *J. Amer. pharm. Ass.*, 1937, 479.

A mixture of 20 parts castor oil and 100 parts shellac dissolved in alcohol was found to be satisfactory.—J. J. Goorley and C. O. Lee, *J. Amer. pharm. Ass.*, 1938, 379.

Mastic-magnesium stearate is recommended for the enteric coating of pills.—F. S. Bukey and C. J. Klemme, *J. Amer. pharm. Ass.*, 1939, 87.

#### **Keratinum (B.P.C.).**

A group of proteins forming the chief constituents of horns, hoofs, feathers, etc., and resistant to enzyme or chemical action. Occurs as a brownish-yellow powder or greyish-white scales.

[P2] **Liquor Keratini (B.P.C.)** is a 10% w/v solution in ammoniacal alcohol. Used for the enteric coating of pills, capsules, etc.

#### **Pulveres pro Pilulis.**

It is often possible to prepare from a formula for a pill mass all the ingredients, with the exception of the excipient, in the form of a powder. This facilitates the preparation of repeated batches of the pills, since one weighing of the compound powder will replace three or more in the ordinary manner of dispensing. The following are the relations by weight between the "*Pulvis pro pilulis*" and the quantity of the excipient, syrup of liquid glucose, necessary to produce a pill mass of suitable consistence.

Pill.	Weight of powder.	Weight of syrup of liquid glucose.
Pil. Aloes	9	1
" Aloes et Asafoet.	9	1
" Aloes et Ferri	33	17
" Aloes et Myrrh.	33	17
" Coloc. et Hyoscy.	43	7
" Galbani Co.	3	1
" Hydrarg. Subchlor. Co.	41	5
" Ipecac. cum Scilla	5	1
" Plumbi cum Opio	41	6
" Rhei Co.	3	1
" Saponis cum Opio	4	1
" Scilla Co.	4	1

## PINUS

**Pinus Alba** (B.P.C.). *Syn.* WHITE PINE BARK. The bark of the Weymouth pine, *P. Strobus* (Pinaceæ).

**Extractum Pini Albi Liquidum** (B.P.C.).

*Dose.*— $\frac{1}{4}$  to 1 drachm (1 to 4 ml.). 1 in 1. Sometimes included in cough syrups.

**Syrupus Pini Albi Compositus** (B.P.C.).

*Dose.*—1 to 2 drachms (4 to 8 ml.).

Liquid extract of white pine, 1 in 20, with syrup of tar, liquid extract of squill and ammonium chloride, in a glycerin-syrup basis.

[P1] **Anodyne Pine Expectorant** (*Parke, Davis, London*). Combination of extracts of white pine, wild cherry, balsam poplar buds, etc., with chloroform 4 m. and morphine acetate  $\frac{1}{2}$  gr. in 1 oz.

**Pinus Canadensis** (B.P.C.). *Syn.* HEMLOCK SPRUCE, PINUS BARK.

The dried inner bark of *Tsuga canadensis* (Pinaceæ). Contains 8 to 15% of tannin.

**Extractum Pini Canadensis Liquidum** (B.P.C.). *Dose.*— $\frac{1}{4}$  to 1 drachm (1 to 4 ml.). 1 in 1. It is used as an astringent in leucorrhœa and given internally for diarrhœa, hæmoptysis and night sweats.

**Pinus Sylvestris.** *Syn.* SCOTCH FIR OR PINE.

From the wood of this tree (principally in America, France and Russia) much of the oleo-resin, common turpentine, oil of turpentine, gum thus or American frankincense, resin or colophony, and wood tar (*vide* *Pix Liquida*) are produced. From its leaves also are prepared an extract and volatile oil.

**Oleum Pini Sylvestris** is a commercial name for the oil distilled from various coniferous leaves and twigs; it is not distilled from *Pinus sylvestris*.

**Oleum Terebinthinæ** (B.P., U.S.P. XI, *P. Helv. V*, *P. Dan.*).

*Syn.* OLEUM TEREBINTHINÆ ÆTHEREUM (*Fr. Cx.*), OLEUM TEREBINTHINÆ RECTIFICATUM, CAMPHINE.

*Dose.*—3 to 10 minims (0.2 to 0.6 ml.). Anthelmintic dose 2 to 4 drachms (8 to 16 ml.).

Is distilled from the oleo-resin, turpentine, obtained from *Pinus sylvestris* and other species of *Pinus*. U.S.P. XI and *P. Helv. V* contain Oleum Terebinthinæ and Oleum Terebinthinæ Rectificatum, the latter to be dispensed when for internal use. *Fr. Cx.*, *P. Helv. V* and *P. Dan.* recognise the oil of *P. maritima* (*P. Pinaster*) only.

**Soluble** 1 in 7 of alcohol 90%; miscible with alcohol 95%, ether, chloroform and glacial acetic acid.

By "Turpentine," i.e., **Terebinthina** (*N.F. VI*, *P. Svec. X* and in other countries), is meant the concrete oleo-resin obtained as exudate from various species of *Pinus*. Synonyms for this natural product are Gum Thus, Thus Americanum and Common Frankincense. **Bordeaux Turpentine** is a variety obtained in S.W. France.

**Antidotes.** Empty stomach by emetic or stomach tube. Give purgative dose of magnesium sulphate. Demulcent drinks. Hot applications to loins. Morphine,  $\frac{1}{4}$  gr. hypodermically, or tincture of opium by mouth, for pain.

Death of a man of 39 following drinking of 6 oz. of oil of turpentine. Lining of stomach completely macerated and lying in small pieces in the gastric cavity. The wall of the stomach felt like leather.—F. P. Maitland, *Brit. med. J.*, ii/1931, 77.

**TURPENTINE IDIOSYNCRASY.** Vesicular eruption, urticaria and vomiting following use of Linimentum Album (B.P.C.) on unbroken skin.—W. W. Jeudwine, *Brit. med. J.*, i/1933, 513.

Idiosyncrasy by no means unusual. Turpentine causes rubefaction and vesiculation on any skin if applied sufficiently concentrated, and will cause this irritation in some individuals in very small dosage, the irritation in these cases not being limited to the site of application, but a papular, urticarial rash, which may become oozing and eczematous, appears at the periphery of the point of contact and may become quite generalised. The application of turpentine to the skin contains a real element of danger.—R. L. Sutton, *Brit. med. J.*, i/1933, 805; J. T. Ingram, *ibid.*, 894.

**Uses.** Oil of turpentine has the therapeutic action of other essential oils. Internally it is carminative, producing a sensation of warmth in the mouth and stomach and assisting the expulsion of flatus. It is excreted especially by the kidneys and lungs, and has been given in cystitis as an antiseptic and for promoting diuresis, and in bronchitis as an expectorant. Large doses are irritant to the bladder and urethra and even small doses may increase a pre-existing inflammation. Given with castor oil to prevent absorption, large doses are administered as a vermifuge for tape-worm. As an enema it is employed to evacuate the bowel, to expel flatus and also to remove tape-worm and thread-worm. Mixed with olive oil it is of value as an enema in the typanites of typhoid fever. Externally it is rubefacient, and is employed in numerous liniments for rheumatism, stiffness, etc., and a turpentine stupe consisting of  $\frac{1}{2}$  to 1 dr. of the oil sprinkled on flannel wrung out of hot water is commonly used as a counter-irritant for the relief of abdominal pain. The oil is an effective hæmostatic, and may be applied on gauze to arrest hæmorrhage from a tooth socket or the nose.

Subcutaneous or intramuscular injections of turpentine are given to promote the formation of a "fixation abscess" in the treatment of various diseases of microbial origin. The oil may be given as a 15% admixture with olive oil, sometimes with the addition of 0.5% each of benzocaine and quinine hydrochloride. The adult dose is 0.5 to 1 ml. every 4 to 7 days; children may receive 4 m., and infants up to 5 years 1 to 2 m. weekly. Increased leucocytosis is produced, and the treatment has been found valuable in septicæmia, erysipelas and other streptococcal infections, also in furunculosis, acne, etc. Fixation abscess treatment may also assist in the isolation of the infecting organisms in infections of unknown origin.

**TYPHOID.** Give 20 m. of turpentine emulsion or a capsule of 5 m. oil of cinnamon 2- or 4-hourly and a  $\frac{1}{2}$  pint ox-gall enema, and apply heat to the abdomen if there is no hæmorrhage.—A. E. Gow, *Lancet*, i/1930, 39.

**Emulsion Olei Terebinthinæ (U.S.P. XI).** Average dose.— $\frac{1}{2}$  drachm (2 ml.). Rectified oil of turpentine 15% with acacia and water.

**Enema Terebinthinæ (B.P.C.).** Dose.—20 ounces (600 ml.). Oil of turpentine 2.5 to 5% v/v in mucilage of starch or in 5% aqueous soft soap.

**Enema Terebinthinæ (St. M.H., St. Mark's H.).** Oil of turpentine  $\frac{1}{2}$  oz., soap enema (1 in 20) to 1 pint. W.H. is the same except that the soap enema is 1 in 40. St. T.H. uses oil of turpentine  $\frac{1}{2}$  to  $\frac{3}{4}$  oz. in  $\frac{1}{2}$  to 1 pint of mucilage of starch. St. G.H. has oil of turpentine 1 oz. in starch enema ( $\frac{1}{2}$  oz. boiled with 20 oz. of water) to 1 pint. Mid. H. has 1 oz. of oil in 20 oz. of simple enema (soft soap 1 oz., water to 1 pint). L.H. is the same, using  $\frac{1}{2}$  to 4 dr. of oil. K.C.H.

uses 1 oz. of oil of turpentine emulsified in milk 2 oz., or yolk of egg, and made up to  $\frac{1}{2}$  to 1 pint with soap enema (1 in 20). *Gt. Orm. H.* uses 2 dr. of oil mixed with 10 oz. of starch mucilage prepared with 2 dr. of starch. *C.X.H.* has oil of turpentine 1 oz., starch enema (1 in 40) to 15 oz.

**Gossypium Terebinthinæ.** *Syn.* TURPENTINE WOOL (*R.D.H.*). Cotton wool or gauze soaked in the oil and squeezed dry, packed into the toothsocket as a stupe.

**Hustus Terebinthinæ** (*St. G.H.*). Oil of turpentine 10 m., tincture of quillaia 10 m., syrup 30 m., cinnamon water to 1 oz.

**Dutch Drops.** *Syn.* HAARLEM DROPS. For lumbago and rheumatism. *Ph. Form* states:—Form now generally adopted in Denmark and Holland is:—Heat to 165° in an iron vessel large enough to allow some frothing, linseed oil 4 and sulphur 1, with stirring until mixture drops off the stirrer with a glassy appearance. Remove from the fire and add 15 parts (by weight) of oil of turpentine, and agitate until solution is complete or nearly so, then filter. The liquid should be limpid and of a brownish-red colour. Has been given in a dose of 5 to 30 m. (0.3 to 2 ml.).

**Linimentum Album** (*B.P.C.*). *Syn.* EGG LINIMENT, WHITE EMBROCATION, LINIMENTUM ALBUM ACETICUM.

An egg emulsion containing about 40% of oil of turpentine and 8% of acetic acid.

**Lin. Album** (*N.I.F.*). *Syn.* LIN. COMMUNE. Soft soap 66 gr., ammonium chloride 11 gr., oil of turpentine  $\frac{1}{2}$  oz., hot water to 2 oz.

**Linimentum Terebinthinæ** (*B.P.*).

Contains oil of turpentine 65% *v/v* with camphor 5% *w/v*, soft soap and distilled water.

Knight's method is satisfactory. Mix solution of potash (*B.P.* '98) 3 oz. with water 3 oz. in a bottle, add oleic acid 7 dr. previously mixed with oil of turpentine 3 oz., and mix gently. To this emulsion add oil of turpentine 10 oz. with camphor 1 oz. dissolved in it, in portions of 1 oz. or more at a time. *Liquor Potassæ* (*B.P.* '98) contained 6-19% *w/v* of KOH.

**Linimentum Terebinthinæ Aceticum** (*B.P.*).

Glacial acetic acid 110 ml., liniment of camphor 445 ml., oil of turpentine to 1000 ml.

**Linimentum Terebinthinæ Aceticum** (*N.F. VI.*). *Syn.* STOKES' LINIMENT, ST. JOHN LONG'S LINIMENT. Oil of turpentine 400 ml., oil of lemon 16 ml., acetic acid 80 ml., yolks of 4 eggs, whites of 2 eggs, water to 1000 ml.

**Linimentum Terebinthinæ Compositum** (*B.V.H.*). Salicylic ester of dihydroxy-ethane 1 oz., oleoresin of capsicum 5 gr., olive oil 2 oz., oil of turpentine to 5 oz.

**Sapo Olei Terebinthinæ.** Turpentine 1, soft soap 2, glycerin 1. As a vermicide—also a stimulant local application.

**Spiritus "Antiparalyticus."** Turpentine oil 4, oil of amber 4, camphorated spirit 64, dilute solution of ammonia 28. Used as a liniment.

**"Sanitas" Fluid** (*Sanitas Co., London*) is prepared by the action of water upon air-oxidised turpentine. It contains as its active principles hydrogen peroxide, thymol, a soluble camphor, and some camphoric acid. A household disinfectant and oxidiser. Non-poisonous, does not stain linen. Is used in midwifery. "Sanitas" Oil has sp. gr. 0.95. A strong oxidising agent. For inhalation in phthisis. Diluted with spirit used as spray in a room, or 1 in 8 to 20 of olive oil for skin affections.

**Terebinthina Canadensis** (*B.P.C.*). *Syn.* CANADA BALSAM, BALSAM OF FIR.

The oleoresin from *Abies balsamea* (Pinaceæ) occurring as a pale yellow, viscid liquid soluble in all proportions of benzene, xylene, chloroform and ether; about 80% is soluble in alcohol

90%. After preparation by warming for some hours in an open dish until a small portion sets to a brittle solid on being cooled, and dissolving the residue in an equal quantity of xylene it is used as a microscopic mounting medium.

**Venice Turpentine** is the oleoresin from *Larix europæa* (Pinaceæ). It is a viscid yellow fluid soluble in dehydrated alcohol.

**Terebinthina Veneta** (*P. Helv. V*), *syn.* TERÉBENTHINE DU MELEZE (*Fr. Cx.*), is from *L. decidua*.

Commercial Venice turpentine is usually a factitious substance.

Soluble 1 in 5 of alcohol, and in ether and chloroform.

**Balsamum Locatelli.** Venice turpentine 18, yellow beeswax 12, olive oil 18, balsam of Peru 2, dragon's blood 1. For chilblains (even if broken).

**Terebinthina Veneta Factitia** (*B.P.C.*). A mixture of colophony, linseed oil and oil of turpentine melted together and allowed to cool.

**Larix** (*B.P.C.*). *Syn.* LARCH BARK.

The bark of *Larix europæa*, containing tannin. **Tinctura Laricis**, *dose.*—20 to 30 minims, 1 in 8, has been used as an expectorant in chronic bronchitis.

**Oleum Pini Pumilionis** (*B.P.C., U.S.P. XI, P. Helv. V*).

*Dose.*—1 to 5 minims (0.06 to 0.3 ml.).

The oil of the leaf of *Pinus Pumilio* (Coniferæ). Is more aromatic than the oil of Siberian fir. It is used for inhalations.

**Syrupus Pini** (*B.P.C.*).

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Contains 1 in 160 of oil of pumilio pine in glycerin, sucrose and water.

[D·P1·81] **Pinheroin** (*Oppenheimer, London*). Preparation containing diamorphine hydrochloride  $\frac{1}{4}$  gr. and terpine hydrate 1 gr. per dr. with essence of Canadian pine, for use as a respiratory stimulant. *Dose.*—1 drachm every 2 or 3 hours if necessary.

**Oleum Abietis** (*B.P.*). *Syn.* OIL OF SIBERIAN FIR, OIL OF PINE. Distilled from the fresh leaves of *Abies sibirica*. Contains 33 to 45% *w/w* of esters calculated as bornyl acetate,  $C_{12}H_{20}O_2$ .

**MOSQUITO LARVÆ AND PUPÆ.** Pine oil has a powerful soporific or paralyzing effect, resulting in their death. A mixture of crude oil and pine oil, in the proportion of 9 parts of the former to 1 of the latter, is effective in destroying all stages of Anopheline and Culicine larvæ and pupæ.

**Olibanum** (*B.P.C., Fr. Cx.*), *syn.* FRANKINCENSE, is the dried oleoresin from *Boswellia Carterii* and other species (Burseracæ). In ovoid yellowish, bluish or greenish tears. Used in incense and fumigating powders.

**Terebenum** (*B.P., U.S.P. XI*).

*Dose.*—5 to 15 minims (0.3 to 1 ml.). *U.S.P. XI* average dose 4 minims.

A colourless liquid consisting of dipentene and other hydrocarbons, produced by the action of sulphuric acid on oil of turpentine and distillation. Sp. gr. 0.862 to 0.870. It has an agreeable odour resembling fresh-sawn pine-wood.

**Soluble** 1 in 5 of alcohol 90% and in all proportions in absolute alcohol or chloroform. It is not miscible with water, but may be emulsified by mixing it with one-sixth its weight of tragacanth powder, then adding water and shaking.

**Uses.** An agreeable antiseptic, disinfectant and deodorant. The vapour is a useful sedative and antiseptic inhalation in whooping cough and chronic bronchitis.



WHOOPIING COUGH cured by 1 to 2 minims on sugar occasionally.—*Lancet*, ii/1929, 34.

**Vapor Terebeni.** Equal parts of terebene, phenol and spirit of chloroform. 10 drops on the pad of an oro-nasal respirator.

[P1] **Bronchol** (*Sharpe & Dohme, London*). Capsules containing terebene 1 m., oil of sandalwood  $1\frac{1}{2}$  m., creosote  $\frac{1}{2}$  m., eucalyptol  $\frac{1}{2}$  m., strychnine  $\frac{1}{100}$  gr., olive oil to 5 m. For bronchitis, bronchial catarrh, etc. *Dose*.—1 or 2 capsules after meals.

**Terpini Hydras** (*B.P.C., U.S.P. XI, P. Ned. V, P. Helv. V*).  $C_6H_8(OH)_2 \cdot CH_3 \cdot C_3H_7, H_2O = 190.2$ . *Syn.* TERPINE (*Fr. Cx.*), TERPENE HYDRATE.

*Dose*.—3 to 10 grains (0.2 to 0.6 g.), in cachets, capsules or pills, or suspended in a mixture.

In prismatic crystals.

**Soluble** 1 in 280 of water, 1 in 32 of boiling water, 1 in 14 of alcohol 90%, 1 in 100 of ether, 1 in 200 of chloroform.

**Uses.** Lessens cough; has been used with success in bronchitis, chronic and subacute; it assists expectoration, e.g., in initial catarrh of phthisis.

**Elixirium Terpini Codeinque Compositum** (*Fr. Cx.*). Terpene 0.5%, codeine 0.1%, brandy 60%, syrup of tolu 34.4%, cherry-laurel water 5%, all by weight.

**Terpinol.** An agreeably aromatic liquid containing various terpenes ( $C_{10}H_{16}$ ), and oxygenated bodies, including terpineol, obtained by the action of dilute sulphuric acid on terpin hydrate. Miscible with alcohol in all proportions, but insoluble in water. Has been given in pulmonary hæmorrhage in 3-drop doses. Is used mainly in perfumery for its hyacinth odour.

**Terpineol.** *Syn.* TERPILENOL.  $C_{10}H_{17}OH = 154.1$ . A colourless viscid liquid obtained by the fractional distillation of terpinol. Used for disguising odour of iodoform and in perfumery, having a lilac odour.

**Terpoflor** (*Wilcox, JozEAU, London*). Contains cedrene, pinene, anethol, camphoric aldehyde, cineole, methyl orthoamidobenzoate, linalyl acetate, terpineol and sesquiterpenes in liquid paraffin. Supplied in gelatin capsules, the contents of which are instilled into the nose. For use in nasal congestion.

## PITUITARIUM

*Syn.* PITUITARY GLAND, HYPOPHYSIS CEREBRI.

[P1] "Pituitary gland, the active principles of."

[S6] "Pituitary gland, the active principles of—specify proportion as either:—

- the number of units of activity as defined in the "British Pharmacopœia" contained in a specified quantity of the preparation; or
- the proportion of pituitary gland, or of anterior or of posterior lobe of the gland, as the case may be, contained in the preparation; or
- the amount of pituitary gland, or of anterior or of posterior lobe of the gland, as the case may be, from which a specified quantity of the preparation was obtained, together with an indication whether the amount relates to fresh or to dried gland substance."

[87] *Medicines made up ready for the internal treatment of human ailments containing—Pituitary gland, the active principles of—must be labelled with the words "Caution. It is dangerous to take this preparation except under medical supervision."*

A small reddish-grey, ductless gland weighing, in man, about 10 grains, situated at the base of the brain in the sella turcica of the sphenoid bone. The average total weight of the gland in the ox is 2·5 g.; the anterior part being 2 g., and posterior 0·5 g.

*Anatomically* the gland consists of the anterior lobe, the *pars intermedia*, the posterior lobe and the *pars tuberalis*. The *pars intermedia* lies between the (larger) anterior lobe and the (smaller) posterior lobe; it is developed in connection with the anterior lobe as an upward growth (Rathke's pouch) of the ectoderm lining the bucco-pharyngeal cavity. The posterior lobe is developed from that portion of the diencephalon which forms the floor of the third ventricle with which it is connected by the neck or infundibulum (a funnel). In man, both neck and body are solid, with traces of a cavity in the neck. The *pars tuberalis* is a thin layer which forms a collar for the infundibulum, and spreads out over a small adjacent part of the base of the brain.

*Histologically* the anterior lobe is composed of irregular columns of cells separated by connective tissue and large vascular sinuses. The cells are differentiated into two groups according to the intensities of the staining reactions of their cytoplasm—chromophobe cells with clear non-granular cytoplasm and chromophil cells with deeply staining granules—further differentiated as acidophil (oxyphil) and basophil cells, according to the affinities of their cytoplasm for acid and basic dyes respectively. The posterior lobe, or *pars nervosa*, is composed of neuroglia cells, fibres and pituicytes, but no nerve cells have been identified in it. In the human pituitary gland the bulk of the tissue of the posterior lobe is made up of larger pyramidal or spindle-shaped cells termed pituicytes, which often contain greenish-brown granules. The *pars intermedia* is closely applied to the *pars nervosa*, and consists of short columns of small polyhedral cells with round, centrally-placed nuclei and granular cytoplasm.

*Physiologically* the resemblance of the minute structure of the anterior portion of the gland to a typical secreting gland is consistent with the production of an internal secretion, but the resemblance of the cells of the *pars nervosa* to those of nervous tissue has led to the suggestion by many investigators that the secretion of the posterior lobe is elaborated in the *pars intermedia*.

The hypophysis and metabolism (with a bibliography containing 437 references).—B. A. Houssay, *New Engl. J. Med.*, i/1936, 961.

*The Physiology and Pharmacology of the Pituitary Body*, by H. B. Van Dyke.

### Posterior Lobe

[P1-87] **Extractum Pituitarii Liquidum (B.P.).** *Syn. and Prop. Names.* SOLUTUM EXTRACTI HYPOPHYSÆ (*Fr. Cx.*), GLANDUITRIN (*Richter, London*), HYPOPHYSIN (*Bayer Products, London*), INFUNDIBULIN (*Evans, Sons, Lescher & Webb, Liverpool*), INFUNDIN (*Burroughs Wellcome, London*), PITIBULIN (*Allen & Hanburys, London*), PITON (*Organon Laboratories, London*), PITOXYLIN (*Oxo, London*), PITUITRIN (*Parke, Davis, London*).

*Dose.*—2 to 5 units (0·2 to 0·5 ml.) by subcutaneous injection.

Pituitary (posterior lobe) extract is prepared with 0·25% acetic acid, and is assayed and adjusted to contain 10 units per ml. and to pH 3 to 4.

The preparation of a stock powder for the manufacture of the official extract when required is described.—H. Gartside, J. Pritchard and F. E. Rynill, *Quart. J. Pharm.*, 1938, 401.

**[P1-87] Liquor Pituitarii Posterioris (U.S.P. XI).**

*Average dose.*—15 minims (1 ml.), by hypodermic injection.

1 ml. produces an activity upon the isolated uterus of the virgin guinea-pig equal to 80 to 120% of that produced by 0.005 g. of a standard powdered posterior pituitary.

**Therapeutic Substances Regulations.** The unit is the activity corresponding to that yielded by 0.5 mg. of the *standard preparation* when extracted by an approved method. The acidity of the aqueous extract shall be not less than pH 4 nor more than pH 3. Samples must be tested for sterility, and the label must indicate the strength (units per ml.), batch number and licence number, and name and address of manufacturer.

The B.P. directs that extracts should not be used when more than 18 months old.

The statement in the B.P. as to the reduction in activity during storage is only correct if the average temperature does not rise above 5°.—F. Wokes, *Pharm. J.*, ii/1932, 476.

**Uses.** The most potent action of pituitary (posterior lobe) extract is its stimulation of smooth muscle. This is especially marked in respect of the uterus, and it is in the stimulation of uterine contractions in obstetrics that this extract finds its most important therapeutic application. In the early days it was used to hasten delivery, but its use for this purpose has now been largely abandoned, since if the cervix is not fully dilated the too powerful contractions may cause rupture of the uterus. It is now mainly employed in the third stage, *i.e.*, after expulsion of the placenta, to produce prompt and firm contraction of the uterus and thus check post-partum hæmorrhage. If it is given before delivery of the child the dose should never be more than 2 units, and then should only be given when the os is approaching full dilatation.

The next most important action of pituitary (posterior lobe) extract from the therapeutic aspect, is its antidiuretic effect, which is attributable to a specific limitation of the water-excreting capacity of the kidneys, resulting in decreased volume and increased concentration. This action is employed with striking effect in diabetes insipidus to relieve the thirst and control the diuresis.

The stimulant effect of pituitary (posterior lobe) extract on the smooth muscle of the intestine, causing increased peristalsis, is made use of in paralytic ileus, where an immediate action of the bowel may follow the injection of  $\frac{1}{2}$  to 1 ml.

Posterior lobe extract, when injected, also produces a rise in blood pressure, due to vasoconstriction, and it may be found of value in minor degrees of shock. It also antagonises the action of insulin (by retarding the peripheral utilisation of the blood sugar) and may be employed in hypoglycæmic coma.

**DIABETES INSIPIDUS.** Pituitary (posterior lobe) causes a marked antidiuretic effect lasting some hours in patients with diabetes insipidus or in normal subjects who have previously drunk large quantities of water.—See W. W. Burgess, A. M. Harvey and E. K. Marshall, *J. Pharmacol.*, 1933, 49, 237. See also I. Gersh, *J. Pharmacol.*, 1934, 52, 231.

Intranasal administration of 1 ml. liquid extract applied with a spray (also by insufflation of powder) successful in many cases of diabetes insipidus.—per *Brit. med. J. Epit.*, ii/1928, 82; also *ibid.*, i/1929, 21.

**HÆMOPTYSIS.** The most effective immediate remedy is the subcutaneous injection of 1 ml. of pituitary (posterior lobe) extract.—W. H. Wynn, *Brit. med. J.*, ii/1934, 833.

**HERPES ZOSTER.** Relief of pain following injection of 1 ml. It appears to act most dramatically when the pain is most intense.—F. H. Gillett, *Lancet*, ii/1934, 307.

Cases of herpes zoster involving branches of the trigeminal nerve and unrelieved by all other forms of treatment obtained relief from the injection of 1 ml. of Pituitrin. The pain disappeared within a few minutes and did not return for 24 hours, when the injection was repeated.—S. H. Portnoy, per *J. Amer. pharm. Ass. (Abstr.)*, 1939, 398.

**LABOUR.** The multipara with the flabby uterus must not be given any oxytocic drug. It is safer for the general practitioner to reserve pituitary extract for the termination of the third stage.—B. Solomons, *Lancet*, ii/1934, 11.

Nasal method of administration safe and efficient for accelerating labour already in progress. Insert a pledget of cotton wool moistened with 20 m. pituitary extract under the anterior end of the inferior turbinate of one nostril, withdraw after an hour or two and, if necessary, apply a fresh pledget to the opposite nostril.—Hofbauer and Hobiner, per *Prescriber*, 1928, 180.

Intravenous injection of pituitary (posterior lobe) extract in doses of 1 minim given in a number of cases; said to be safe. Best results when given after the membranes have ruptured and in secondary inertia, before full dilatation or with full dilatation when the head is on the perineum; results also good in post-partum hæmorrhage and after cæsarean section.—H. A. Barron, *J. Obstet. Gynec.*, 1935, 322. See also *Lancet*, i/1935, 1398.

There is not sufficient advantage to justify the routine use of pituitary extract in the third stage of labour.—B. L. Williams, *Proc. R. Soc. Med.*, 1939, 32, 920. The intramuscular use of 5 units of Pituitrin directly after the birth of the child showed: (1) that duration of the third stage is not appreciably affected, (2) the average loss of blood is less, (3) the incidence of post-partum hæmorrhage is less, (4) there is no tendency for chorion to be retained, (5) there is no tendency for contraction ring to form, (6) there is no case of Pituitrin shock.—R. C. Percival, *ibid.*, 923. The average duration of labour is slightly shorter in cases where Pituitrin is given, the incidence of post-partum hæmorrhage of over 20 ounces is not reduced, and there is a danger of hour-glass spasm of the uterus.—S. G. Clayton, *ibid.*, 926.

As the result of an experiment covering over 1000 consecutive cases, with a similar number of controls, it was concluded that there is no danger whatever in giving 1 ml. (10 units) of Pituitrin (or Pitocin) during the third stage of labour, and that the amount of hæmorrhage is not much affected, though there was a tendency to a smaller post-partum loss in the Pituitrin cases. It is not claimed, however, that posterior pituitary extract should be given in the third stage as a routine treatment for all cases, nor should control of the fundus, or the very watchful care necessary at this stage, be relaxed or be replaced by any oxytocic drug.—G. W. Blomfield, *Brit. med. J.*, ii/1938, 1083.

**PARALYTIC ILEUS.** Pituitary (posterior lobe) intravenously extremely valuable, given in a dose of 0.5 to 1 ml. into the median antecubital vein very slowly (0.1 ml. every 5 seconds). Dramatically sudden result in every one of three cases.—F. F. Rundle, *Brit. med. J.*, ii/1935, 1208.

Description of three further cases successfully treated.—S. O. Aylett, *Med. Pr.*, 1938, 386.

**POST-PARTUM HÆMORRHAGE.** In cases of post-partum hæmorrhage, pituitary (posterior lobe) extract should be injected into the fundus uteri through the abdominal wall, provided the bladder is empty. The uterus must be compressed bimanually, a fist being inserted into the anterior fornix and the external hand behind the organ pressing it forwards and upwards.—W. F. Rawson, *Brit. med. J.*, i/1935, 1317.

**Hypersensitiveness to pituitary extracts** occurs in only a small percentage of persons. The constituent of the extract responsible is neither the vasopressor nor the oxytocic principle. The symptoms are usually swelling of the face and hands with urticaria.—Senior and Ryder, *J. Amer. med. Ass.*, i/1936, 512.

Spasm of the cervix which on rare occasions occurs with retention of the placenta after the proper use of pituitary extract may be relieved by injection, of 5 m. of adrenaline solution 1 : 1000.—G. G. Copeland, *Canad. med. Ass. J.*, i/1936, 317.

### SOME PROPRIETARIES CONTAINING PITUITARY (POSTERIOR LOBE) EXTRACT

[P1-87] **Lysasthmin** (*Richter, London*). Glanduitrin (posterior pituitary extract) 0.5 ml., adrenaline (1 in 1000) 0.5 ml. *Dose*.—0.5 to 2 ml. subcutaneously or intramuscularly. Bronchial asthma, cardiac and renal dyspnoea, etc.

[P1-87] **Pitalin** (*Paines & Byrne, London*). Ampoules of 1 ml. contain 5 units of pituitary (posterior lobe) extract and 0.5 mg. of adrenaline. *Dose*.—1 ampoule repeated as necessary. Asthma.

[P1-87] **Pitrphorin** (*Schering, London*). Pituitary posterior lobe extract for intramuscular or subcutaneous injection (1 ml. contains 10 i.u.). Menorrhagia, post-partum hæmorrhage, induction of labour, intestinal atony.

[P1-87] **Pituchinol** (*Camden Chemical Co., London*). Pituitary (posterior lobe) extract and quinine base. Ampoules contain 1 ml. = 3 units of pituitary extract and 1 g. of quinine. Stimulating and regularising uterine contractions in all stages of labour.

#### *Active Principles of the Posterior Lobe.*

From the posterior lobe of the pituitary gland, two extracts with different effects have been separated, the oxytocic or uterine-stimulating principle, and a vasopressor principle which elevates the blood pressure, stimulates the bowel, particularly the colon, and inhibits diuresis. It is not yet certain whether there is a third principle affecting carbohydrate metabolism. The oxytocic and vasopressor principles have been markedly concentrated and nearly completely separated from each other, but are not yet available as pure substances. Study of these concentrated preparations has led to the conclusion that the two active principles are amines.

A practical advantage arising from the separation of the oxytocic principle from the vasopressor principle is that the effect of pituitary extract on uterine muscle can be obtained without the simultaneous occurrence of changes in blood pressure. It happens very occasionally that the administration of pituitary extract is followed by the collapse of the patient apparently caused by a fall in blood pressure. So far as is known this fall is due to the vasopressor principle, and therefore in using the oxytocic principle no danger of such a collapse can arise.

Evidence is offered that mild insulin hypoglycæmia in dogs can be completely abolished by small doses of oxytocic hormone of the posterior lobe of the pituitary; corresponding doses of the pressor fraction have little or no effect. Larger doses of the oxytocic hormone not only abolish the insulin effect, but cause a rise in the blood-sugar level above normal.—H. C. Ellsworth, *J. Pharmacol.*, 1936, 56, 420.

Blood pressures and intestinal actions of pituitary (posterior lobe) extract, injected intravenously in the unanæsthetised dog, vary markedly with the fraction used, even when equal pressor-assayed dosages are employed. The presence of the oxytocic hormone may inhibit or abolish the typical effects of the pressor constituent. It is thus concluded that the pressor hormone *per se* causes, under such conditions, a fall of blood pressure, stimulation of intestinal activity, and defecation; while the oxytocic constituent *per se* in sufficient dosage exerts a definite antagonistic influence in respect of these actions. These observations may explain some of the conflicting reports on the clinical usefulness of the agents in question.—K. I. Melville, *J. Amer. med. Ass.*, 1/1936, 105.

**The Oxytocic Principle** of the posterior lobe of the pituitary has been named oxytocin or  $\alpha$ -hypophamine. It affects the muscle of the uterus in child-birth, causing increased rate of

rhythmic contraction, improving the tone, and ensuring that the uterus remains contracted after delivery, thus preventing post-partum hæmorrhage.

[P1-57] **Orasthin** (*Bayer Products, London*). Oxytocic principle of the posterior pituitary in 1 ml. ampoules containing 3 Veeglin units.

[P1-57] **Pitocin** (*Parke, Davis, London*). Solution of the oxytocic principle containing 10 i.u. per ml. and available in 0.5 or 1 ml. ampoules.

**The Vasopressor Principle** of the posterior lobe of the pituitary gland has been called vasopressin or  $\beta$ -hypophamine. Its action can be divided into three main parts, one elevating the blood pressure, one stimulating the intestine, and a third inhibiting diuresis. Whether these three properties are due to separate substances is not yet known, many investigators believing that the most potent preparations with vasopressor effects are the most potent preparations with anti-diuretic effect.

The pressor property causes elevation of the blood pressure by a direct stimulant action on the smooth musculature of the small arteries and arterioles, whereby the muscle contracts and reduces the diameter of the vessel and so raises the blood pressure. It may also cause constriction of the capillaries and venules. This property is used when the blood pressure is unusually low after surgical operations. The vasopressor principle is most important, however, not for its pressor action, but because it brings about water retention. This property is used to relieve the symptoms of diabetes insipidus, which is characterised by a large intake and output of water. Injections of pituitary extract diminish the excretion and consequently the thirst. The power possessed by the pressor principle of stimulating peristalsis is used in post-operative or paralytic ileus. Injection of large quantities of vasopressin produces a severe hæmorrhagic lesion in the acid-bearing areas of the stomach, caused essentially by inhibition of the gastric secretion. It is also said to produce marked transient impairment of the heart, an effect which may be lessened or prevented by ephedrine, histamine, morphine, nitrites or papaverine.

Doses of 1 ml. of Pitressin intramuscularly, repeated every 4 hours up to 8 or 12 doses, the first dose being given directly following operation, recommended for the prevention of post-operative intestinal distension in abdominal operations.—Potter and Müller, *Ann. Surg.*, 1932, 96, 364.

Pitressin found more effective than the use of enemas for elimination of confusing gas shadows during cholecystography. Report of 73 cases.—Collins and Root, *J. Amer. med. Ass.*, ii/1936, 32.

Pitressin greatly aids in the elimination of obscuring intestinal flatus for the production of better cholecystograms. There is no appreciable alteration in blood pressure or pulse rate following intramuscular injection of 1 ml. (20 pressor units), but it should be used with caution and is contraindicated in cardiac disease, especially coronary disease, arteriosclerosis, hypertension and old age if the vascular system is weakened; also in post-operative cases in which the probability of thrombus or embolus formation is enhanced by possible slowing of the blood stream, and in the later months of pregnancy.—B. R. Kirklin *et al.*, *Proc. Mayo Clin.*, 1939, 502.

The action of the uterine muscle to pituitary preparations is markedly affected by the nature of that ovarian, placental or anterior pituitary hormone whose influence is predominant at the time of injection. During the early stages of pregnancy the human uterus does not react to Pitocin, probably because of the inhibitory effect of the luteal secretion. It does, however, respond to small

doses of Pitressin; whether this is an effect of the drug *per se* or is due to mechanical factors remains a moot point. Later in the gestation period the reactivity to Pitocin returns, and during parturition the uterus is very reactive to this substance, and also to solution of pituitary.—E. M. K. Geiling, *J. Amer. med. Ass.*, i/1935, 738.

**DIABETES INSIPIDUS.** The active principle, vasopressin, is absorbed through the nasal mucous membrane. It can be administered as a spray, or on a pledget of cotton wool soaked in pituitary extract and placed in contact with the turbinates, or as a snuff containing the finely powdered dry gland. The snuff taken every four hours controls diuresis quite satisfactorily. Occasionally it causes asthma, and should then be replaced by a snuff consisting of vasopressin 1% in lactose.—O. Leyton, *Brit. med. J.*, ii/1936, 1042.

[P1-S7] **Pitressin** (Parke, Davis, London), formerly known as vasopressin, a solution of the pressor principle containing 20 pressor units per ml. 1 pressor unit is the pressor activity exhibited by 0.5 mg. of international standard pituitary (posterior lobe) powder.

[P1-S7] **Tonephin** (Bayer Products, London). Vasopressor principle of the posterior pituitary in 1 ml. ampoules, representing 5 Voegtlin units.

**Pitressin Tannate.** A water-insoluble chemical combination of a pressor fraction of the posterior lobe of the pituitary with tannic acid. The pressor fraction is precipitated with tannic acid and the precipitate removed by filtration and washed and dried. Five pressor units of Pitressin tannate are suspended in 1 ml. of peanut oil, the pH of the solution being that of oil. The subcutaneous injection of 1 ml. of the solution controlled the symptoms of diabetes insipidus in three patients for periods varying from 30 to 82 hours without giving rise to disagreeable side-effects.—J. A. Greene and L. E. January, *J. Amer. med. Ass.*, ii/1940, 1183.

**Intermedin.** The hormone of the *pars intermedia* which acts on the chromatophores of cold-blooded animals.—B. Zondek, *J. Amer. med. Ass.*, i/1935, 637.

J. H. Collip and D. K. O'Donovan, with a number of other workers, have discovered a new metabolic factor which can be separated from all the other pituitary ones except the melanophore hormone and which therefore probably comes from the *pars intermedia*. It raises the basal metabolic rate even in the absence of the thyroid and lowers the respiratory quotient. This latter fact implies that the increased metabolism is at the expense of the fat, which suggests its use in the treatment of obesity. It may be the ketonic factor previously attributed to the anterior lobe, since it excites ketonuria in fasted rats, and in dogs, without pancreas or pituitary. It also seems to play a large part in the regulation of carbohydrate metabolism.—*Med. Annu.*, 1940, 364.

A new extract of the pituitary, known as No. 622, and found by O'Donovan and Collip to increase the metabolism of animals, was also found to increase the rate of metabolism in man. The increase of metabolism occurs to an appreciable extent at the expense of fat. The possible uses of this extract in the treatment of obesity, and in conditions where an increase of metabolism is desirable, are now being investigated.—I. M. Rabinowitch and Co-workers, *Canad. med. Ass. J.*, i/1939, 105.

### Anterior Lobe

**Functions of the Anterior Lobe.** For the most part, the data show that the anterior lobe of the pituitary gland is the most important division of the pituitary body in mammals. Through its hormones it appears to touch nearly all the physiological processes of the vertebrate organism, some more profoundly than others. The growth processes, the ovarian and testicular activities seem most completely under pituitary-hormone control. The rest of the endocrine system and the processes of metabolism are less deeply affected, while the nervous system is the least influenced, according to present information. This is partly shown by the

effect of the removal of the pituitary gland (hypophysectomy) from the body; this produces immediate changes in the gonads, the suprarenal cortex and the thyroid, and possibly also in the parathyroid and the islets of Langerhans in the pancreas, and causes cessation of growth.

It is impossible to state how many hormones are *secreted* by the pituitary gland. By means of various crude or refined physico-chemical manipulations many extracts differing in their physiological or pharmacological effects have been obtained. The number of such extracts, however, cannot be taken to correspond to the number of hormones actually elaborated by the pituitary body, and indeed many of the pituitary-gland products have not yet been shown to be true pituitary-gland hormones, that is, secreted into the body fluids by this gland in health or disease. It is now recognised that the application of various physical and chemical processes to the isolated pituitary may give rise to the development of specific chemical entities which are not secreted as such by the gland *in situ*.

At the present time the controlling hormones which appear to emanate from the anterior lobe of the pituitary include a growth hormone, a gonadotrophic hormone, a thyrotrophic hormone, a lactogenic hormone and a suprarenal-cortical-stimulating hormone. In addition to these there are factors affecting the carbohydrate metabolism and the functioning of other glands such as the parathyroid and the thymus. None of these substances has been isolated and their existence as definite chemical entities is open to doubt. The properties of the active extracts so far prepared suggest that either the true hormones are protein-like, or that they are closely associated with protein-like substances. Some investigators believe that they may in part be cleavage products of one or more larger molecules.

Much has been written concerning "anti-hormones," substances which are said to be secreted in the body in response to repeated injections of preparations of pituitary hormones. It has been found, for example, that gonadotrophic, thyrotrophic and growth-stimulating extracts, among others, all cause the production of substances which circulate in the blood and antagonise the effects of pituitary extracts. With the gonadotrophic extracts equally good evidence has been produced to show that such substances are not found in response to gonadotrophic hormones secreted by the intact gland.

The least encouraging aspect of the situation to-day is the clinical application of the experimental findings in the pituitary field. These findings have improved the diagnosis of pituitary disorders in man, but have added little to their control. This may be due in part to the complexity of the pituitary hormone relationships, and in part to the relative inactivity of the hormone preparations administered orally. Greater success in the therapeutic field is dependent upon the greater production of purer preparations for parenteral administration.



The following are some of the physiological effects that have been ascribed to anterior lobe extracts, determined in many instances by the response of normal as well as of hypophysectomised animals: (1) A specific stimulus to general bodily growth. (2) A thyrotrophic action, illustrated by (i) the restoration to normal of the atrophic thyroid of the hypophysectomised animal; (ii) the production of hyperplasia in the thyroid of a normal animal; (iii) the increase in metabolism of the hypophysectomised or normal animal. (3) A gonadotrophic effect shown by the acceleration in the rate of development of the gonads of either sex, as seen for example in immature rats treated with potent extracts. (4) An adrenotrophic or corticotrophic effect demonstrated by the restoration of the suprarenal cortex to normal in the hypophysectomised rat, or a cortical hypertrophy in immature animals treated under well-controlled conditions. (5) A mammary secretagogue action or prolactin effect, best demonstrated by the stimulation of the crop gland in the immature dove or pigeon. (6) A diabetogenic action, shown by the production in dogs of a state quite comparable to pancreatic diabetes, in which there is hyperglycaemia, glycosuria, ketosis and an increased nitrogen elimination in the urine. (7) A ketogenic effect, best demonstrated by the production of ketonaemia and ketonuria in the fasted male rat. (8) An increase in liver fat. (9) A decrease in blood lipoids. (10) An increased secretion of insulin (pancreatrophic effect). (11) Lowering of the respiratory quotient. (12) Increase in metabolism in the thyroidectomised animal. (13) Inhibition of insulin hypoglycaemia (contra-insulin effect). (14) Inhibition of adrenaeline hyperglycaemia. (15) Retention and increase of the carbohydrate stores (glycostatic and glycotrophic effects). (16) Chromatophore and erythrocyte expanding effect (melanophore hormone and intermedin of Zondek, probably produced entirely in the *pars intermedia*).

The number of apparent specific physiological effects of anterior lobe preparations is remarkable, but in view of the fact that there are only three different cell types in the gland, it is highly improbable that the number of individual hormone substances elaborated by the normal functioning gland can greatly exceed the number of cell types. It is suggested that some if not all of the active principles of the anterior lobe exist as prosthetic groups in a very few individual protein substances. The process of secretion from the normal intact gland could then consist in either the liberation of massive protein molecules, each containing active groups of specific hormone nature, or the liberation of the active groups themselves from mother molecules by enzymatic or other action. Until such time as anterior lobe hormones can be identified in and separated from the circulating blood, the true nature of anterior lobe secretion cannot be determined.—J. B. Collip, *Edinb. med. J.*, 1938, 783.

**Anti-hormones.** If the thyrotrophic hormone is injected into an animal, the basal metabolic rate rises, stays up for some days, then falls, and however much is then given no further rise occurs. The falling-off in action is due to the secretion of an anti-thyrotrophic hormone. Similar anti-hormones have so far been prepared also for the gonadotrophic, ketogenic and growth fractions.—E. C. Dodds and R. L. Noble, *Brit. med. J.*, ii/1936, 824. (See also under Thyroid.)

An antidiabetogenic effect of a primary alcoholic extract of pituitary tissue administered orally.—J. B. Collip, *Canad. med. Ass. J.*, i/1940, 109.

### **Active Principles of the Anterior Lobe.**

**The Growth Hormone.** *Syn.* PHYONE. It is now well known that removal of the pituitary gland from young and growing animals markedly inhibits growth. Injection into such animals of preparations of the so-called "growth hormone" causes a resumption of growth. Furthermore, in view of the fact that over-secretion of the anterior lobe of the pituitary in man before completion of growth produces gigantism, or after completion produces acromegaly, it is to be expected that growth at a faster rate and beyond the normal could be brought about by administration of pituitary. In certain animals both of these expectations have been realised. The pituitary in fact, among the endocrine glands, is the most important regulator of growth, but whether this action is due to a

specific growth-promoting hormone is not yet known. It has been suggested that the action is due to the lactogenic hormone, and again to the combined action of the lactogenic and thyrotrophic hormones, but it is significant that although hypophysectomised rats are very sensitive towards the growth-promoting extracts of the pituitary gland, no investigator has yet succeeded in causing such animals to grow by administering either lactogenic hormone or thyrotrophic hormone, or a combination of the two. The maximum effect on the growth of dwarfed mice has been obtained by administering a growth-promoting extract ("Phyone") which was only partially purified and contained lactogenic, thyrotrophic and gonadotrophic hormones. Some authors have reported success in extracting from the anterior lobe of the pituitary, a growth-promoting principle free from gonadotrophic and lactogenic hormones.

A method of preparing a potent, non-irritating phyone extract suitable for clinical use.—H. B. Van Dyke and Z. Wallen-Lawrence, *J. Pharmacol.*, Dec., 1930, 413.

Treatment of endocrine dwarfism with growth hormone from the anterior pituitary gland.—W. Englebach and R. L. Schaefer, *Endocrinology*, 1934, 18, 387.

The growth hormone of the anterior pituitary.—H. M. Evans, *J. Amer. med. Ass.*, 1/1935, 1232.

Growth factor of the anterior hypophysis.—*Lancet*, 1/1935, 505.

There exist in the pituitary, not only the somatotrophic growth hormone discovered by Evans, but also other growth-controlling substances, namely, in the anterior lobe a growth-stimulating, and in the posterior lobe a growth-inhibiting substance. It is suggested that the latter be named "amicine." The growth-stimulating substance accelerated the growth of normal young animals compared with controls under the same conditions. The growth-inhibiting substance from the posterior lobe antagonised this effect, and two or three months later the treated animals were only slightly heavier than the controls, and were also quite normal. The substances were extracted by acetone.—B. Lustig and H. K. Wachtel, *Nature, Lond.*, 1939, 602.

[P1-57] **Antuitrin "Growth"** (*Parke, Davis, London*). Preparation of the growth hormone obtained from anterior pituitary, standardised to contain 10 rat-units per ml. *Dose*.—Single doses of 2 to 5 ml. hypodermically, the weekly dosage varying from 6 to 10 ml.

[P1-57] **Krescone** (*Paines & Byrne, London*). 1 ml. ampoules containing the growth hormone from 2 g. of fresh anterior pituitary. *Dose*.—1 ml. every other day, alternated with 1 ml. of anterior pituitary extract.

**The Gonadotrophic Hormone.** Anterior pituitary secretion is necessary to the normal functioning of the gonads of all classes of vertebrates. Removal of the pituitary body is followed by the cessation of the oestrus cycle in the female animal, and diminution in size of the external genitals of the male; in course of time the secondary sexual characters atrophy completely in both male and female. This can be treated by implantation of anterior lobe in the hypophysectomised animal or, alternatively, by injecting suitable extracts of the anterior lobe. Many attempts have been made to separate the gonadotrophic principle, and although partial purification has apparently been achieved, it is not yet possible to enumerate satisfactorily the different fractions of this principle. Evidence points to the presence of two gonadotrophic hormones, one facilitating follicle-growth and maturation (follicle-stimulating hormone or prolan A), the other promoting the conversion of the

cells of the membrana granulosa and theca into lutein cells (luteinizing hormone or prolán B). Both hormones are said to be necessary to produce ovulation. There is evidence also that these two hormones have an action on the male sex organs, the follicle-stimulating hormone maintaining spermatogenesis in the testis, whereas the luteinizing hormone acts upon the testicular interstitial cells, causing them to secrete the male sex hormone.

Separation of the two constituents (prolán A and B) has recently been attained. In the male infant animal, prolán A is apparently without effect, but prolán B has a strong stimulant effect on the development of the penis, the descent of the testes and on the seminal vesicles.—*Brit. med. J.*, i/1935, 426.

The gonadotrophic hormone is very similar to the thyrotrophic in many ways. Potent extracts may be prepared in exactly the same manner, but to obtain a product high in gonadotrophic activity and relatively low in thyrotrophic substance, one uses sheep anterior lobes, whereas cattle pituitaries serve best for the preparation of thyrotrophic extracts. The stability of the gonadotrophic hormone to heat and varying pH are in general of the same order as for the thyrotrophic hormone.—J. B. Collip, *Edinb. med. J.*, 1938, 791.

**Gonadotrophic Factors from other Sources.** Gonadotrophic substances similar to the principle obtained from the anterior lobe of the pituitary gland are also derived from sources other than the pituitary, and have been termed anterior-pituitary-like hormones. Perhaps the most important are those obtained from the blood serum of pregnant animals and the placenta and urine of pregnant women. These hormones are not secreted by the anterior lobe of the pituitary, but probably originate in the epithelial cells of the chorion, and their effects differ in one or more ways from those of gonadotrophic hormones secreted by or extracted from the anterior lobe.

**The Gonadotrophic Factor from Human Pregnancy Urine.** Human pregnancy urine contains a gonadotrophic substance whose action in the main is luteinising, although it also contains an interstitial-cell-stimulating factor. Most recent observations support the view that this substance, which is commonly referred to as prolán, is secreted by the chorionic cells of the placenta. The best commercial source is still the urine of pregnant women, the largest amounts being secreted in the first months of pregnancy, especially about 50th to 60th day following the last menstrual period, when an enormous secretion is observed. It is in addition, widely distributed throughout the tissues and body fluids of the mother. Following placental death, abortion or normal delivery, the amount of prolán in the urine diminishes rapidly, and may disappear in less than a week after pregnancy. Many investigators consider prolán to be a mixture of the two gonadotrophic hormones, prolán A and prolán B.

The International Unit for the gonadotrophic substance of human urine of pregnancy (chorionic gonadotrophin) has been defined as the specific gonadotrophic activity of 0.1 mg. of a standard international preparation which is dispensed in tablets, each containing approximately 100 international units. The standard substance has an activity similar to that required under

the conditions used by many workers to cause cornification of the vaginal epithelium of the immature rat.

**The Gonadotrophic Factor from the Blood-Serum of Pregnant Mares** differs in several respects from that of human pregnancy urine. Considerable quantities are present in the serum only during a limited part of the gestation period, approximately between the 40th to the 80th day. It is not excreted in significant amounts in the urine even at times when its concentration is highest in the serum, and as might be inferred, it is only slowly metabolised, so that the administration of a single dose, during a period of several days, may be as effective as repeated doses. The hormone which is secreted by the endometrium, as well as by the chorionic epithelium, is far more complete in its gonadotrophic effects than is that obtained from pregnancy urine. Whereas the latter is chiefly a hormone facilitating the growth and function of lutein tissue in the ovary or of the interstitial cells of the testis, the gonadotrophic principle of pregnant-mare serum resembles anterior pituitary gonadotrophic principles in respect of the adequacy and completeness of its effects. The chorionic-endometrial hormone of the pregnant mare can maintain the gonads of male and female animals from which the pituitary gland has been removed, and therefore affects the follicles, corpora lutea, and interstitial tissue of the ovary, or the interstitial cells and germinal epithelium of the testis. This hormone appears to have much greater promise as a therapeutic agent than that of pregnancy urine, both because its gonadotrophic effects are more nearly complete, and because it is remarkably slowly metabolised, apparently not being excreted but only undergoing a slow destruction.

The International Unit for the gonadotrophic substance of pregnant mares' serum has been defined as the specific gonadotrophic activity contained in 0.25 mg. of the standard preparation which is dispensed in tablets, each containing 100 international units.

**Uses of the Gonadotrophic Factors.** Most of the early clinical work on the gonadotrophic factors was conducted with extracts prepared from human pregnancy urine. It was assumed that these represented the whole of the gonadotrophic principle of the anterior pituitary, but their therapeutic effectiveness in the female was subsequently found to be limited to their action on the second phase of the menstrual cycle, *i.e.*, to their luteinising action, and in the male to the development of the connective tissue elements of the testis and the structures associated with its natural descent into the scrotum. Their main indications therefore are in threatened or habitual abortion and in the treatment of undescended testis, in both of which conditions they are reported to have given good results.

More recent work, conducted with the factor obtained from pregnant mares' serum, indicates that this has a more complete

gonadotrophic action than the factor from human pregnancy urine. In the female it exerts a follicle-stimulating action, and in the male it controls spermatogenesis and the development of testicular tissues. It therefore has a wider range of indications than the factor obtained from human pregnancy urine; these indications include sterility in the male, when due to azoospermia, and in the female, when due to ovarian insufficiency; amenorrhœa, due to insufficient ovarian stimulation; cryptorchidism; and pituitary infantilism.

**TEST FOR PREGNANCY.** The presence of the gonadotrophic substance in urine is used as the basis of the well-known Aschheim-Zondek test for pregnancy. The urine is injected in a dose of 0.2 to 0.4 ml. into immature female mice twice daily for three days. The mice are then killed and their ovaries examined for the presence of blood-filled follicles and corpora lutea. If they are present, the woman from whom the urine was obtained is pregnant.

**ABORTION.** In habitual abortion, 100 rat units twice weekly from second to fifth month of pregnancy.—A. Bourne, *Practitioner*, ii/1933; also L. Williams, *Lancet*, ii/1935, 796.

In seventeen pregnancies under urinary prolan, in women who previously had had fifty-one successive pregnancies ending in abortion, stillbirth, or early neonatal death, fifteen ended in the birth of a surviving child—i.e., a 100% failure was transformed into an 88.2% success. There is evidence that vitamin E plays a part in the prolan-progesterone mechanism of pregnancy.—James Young, *Brit. med. J.*, i/1937, 953.

**CRYPTORCHIDISM.** Treatment with gonadotrophic extract of anterior lobe of pituitary glands caused descent of the testes in 12 out of 17 cryptorchid boys.—Werner and co-workers, *J. Amer. med. Ass.*, i/1936, 1541.

Six injections of Pregnyl to enlarge the testis are recommended before operation and 12 injections to prevent atrophy after operation.—E. McLellan, *Lancet*, i/1936, 999.

Spontaneous descent occurs by the seventeenth year in 87% of cases, and treatment with gonadotrophic hormone should be withheld until after the age of 16.—P. Williams, *Lancet*, i/1936, 426.

Successful results obtained by doses of 500 rat units of hormone intramuscularly twice weekly; an account of 33 cases; period of treatment ranged from two weeks to 14½ months.—Spence and Scowen, *Lancet*, ii/1935, 1335; see also *Proc. R. Soc. Med.*, 1935, 427.

18 boys aged from 1½ to 17 years were treated with injections of anterior pituitary-like hormone, the dose usually given being 200 rat units three times a week. Descent occurred in 4 within one month, in all of which the testis was in the inguinal canal before treatment. In 1 the testis returned to the inguinal canal on cessation of treatment. In the remainder treatment failed even when continued for an average of 5 months. At subsequent operation in 7 cases, anatomical factors preventing descent were found, but the treatment was considered to have made operative procedures less difficult.—W. O. Thompson *et al.*, *Endocrinology*, 1937, 220. See also A. J. Cramer, *ibid.*, 230.

The effect of the anterior pituitary-like principle from the urine of pregnant women in the treatment of undescended testes appears to be exaggerated. With 38 patients of all ages descent was produced in only 10 of 50 undescended testes, or in 20% compared with an average of 61% of successful results reported in the literature. In the majority of cases of true undescended testes operative procedures are still necessary because of mechanical factors which prevent descent. It is possible that this material causes descent only of those testes which would descend without treatment about the time of puberty.—W. O. Thompson and N. J. Heckel, *J. Amer. med. Ass.*, i/1939, 397.

**STERILITY.** Two cases of sterility in males in which spermatogenesis followed administration of gonadotrophic hormone from pregnancy urine. Dose.—100 rat units weekly.—V. E. Lloyd, *Lancet*, i/1936, 474.

## PREPARATIONS OF GONADOTROPHIC FACTORS

**From Pituitary.**

[P1-87] **Ambinon A** (*Organon Laboratories, London*). 1 ml. ampoules of Ambinon solution equivalent to 100 to 300 guinea-pig units of thyrotrophic hormone and 50 rat units of pituitary gonadotrophic hormone, packed with ampoules containing 100 i.u. of Pregnyl powder, the latter to be dissolved in the former just before administration. **Ambinon B** consists of 1 ml. ampoules of Ambinon solution alone.

[P1-87] **Glanduantin** (*Richter, London*). Dry ampoules, with ampoules of solvent, containing 100 rat units of the gonadotrophic fraction of the anterior pituitary.

[P1-87] **Gonadotraphon** (*Paines & Byrne, London*). Dry ampoules containing 100 or 500 rat units of the gonadotrophic hormone from the anterior pituitary. Tablets containing 100 or 200 rat units and capsules containing 500 rat units are also available.

**From Pregnancy Urine.**

**Antoxylin S** (*Oxo, London*). Dry ampoules, with ampoules of saline, each containing 100 or 500 rat units of anterior pituitary-like hormone from pregnancy urine.

**Antuitrin S** (*Parke, Davis, London*). *Syn.* ANTROIDIN. 10 ml. vials containing 100 rat units per ml., and 5 ml. vials containing 500 rat units of anterior pituitary-like hormone from pregnancy urine.

**Atregone** (*Abbott Laboratories, London*). Anterior pituitary-like chorionic gonadotrophic hormone from human pregnancy urine, standardised to contain 166 i.u. in each ampoule.

**Gonadotraphon S** (*Paines & Byrne, London*). Dry ampoules, with ampoules of solvent, containing 100 or 500 rat units of anterior pituitary-like hormone from pregnancy urine.

**Gonan** (*British Drug Houses, London*). Dry ampoules, with ampoules of solvent, containing 100 or 500 i.u. of anterior pituitary-like hormone from pregnancy urine.

**Physostab** (*Boots, Nottingham*). Dry ampoules, with ampoules of solvent, containing 100 mouse units of anterior pituitary-like hormone from pregnancy urine.

**Pregnyl** (*Organon Laboratories, London*). Dry ampoules, with ampoules of solvent, containing 30, 100, 500 and 1500 i.u. of anterior pituitary-like hormone from pregnancy urine. Also available in tablets containing 100 or 500 i.u.

**Prolan** (*Bayer Products, London*). Dry ampoules, with ampoules of solvent, containing 100, 500 or 2000 i.u. of anterior pituitary-like hormone from pregnancy urine.

**From Pregnant Mares' Serum.**

**Antostab** (*Boots, Nottingham*). Dry ampoules, with ampoules of solvent, each containing 100 mouse units (equivalent to 200 rat units) of gonadotrophic hormone from pregnant mares' serum.

**Gestyl** (*Organon Laboratories, London*). Dry ampoules, with ampoules of solvent, each containing 40 "double ovarian weight rat units" of gonadotrophic hormone from pregnant mares' serum.

**Gonadyl** (*Roussel Laboratories, London*). Dry ampoules, with ampoules of solvent, each containing 40 Evans units (about 400 mouse units of follicular maturation) of gonadotrophic hormone from pregnant mares' serum.

**Luteoantin** (*Richter, London*). Dry ampoules, with ampoules of solvent, each containing 100 or 400 rat units of gonadotrophic hormone from pregnant mares' serum.

**Serogan** (*British Drug Houses, London*). Dry ampoules, with ampoules of solvent, each containing 200 or 1000 rat units of gonadotrophic hormone from pregnant mares' serum.

**The Thyrotrophic Hormone.** One of the impressive effects of removal of the pituitary body in animals is a marked fall of the

rate at which heat is produced. This change is due principally to inadequate functioning of the thyroid gland, and can be correlated with morphological changes in the thyroid, undischarged colloid accumulating in vesicles lined by flat "inactive" epithelial cells. A specific substance called the thyrotrophic hormone is secreted only by the anterior lobe of the pituitary. It is responsible for the maintenance of the normal thyroid function, and may be important in disorders attributed to deficient or excessive thyroid secretion. Removal of the thyroid gland from animals causes enlargement of the anterior lobe of the pituitary, and it is found that persons with large parenchymatous goitres have enlarged anterior pituitaries. The most significant action of the thyrotrophic hormone is to facilitate or promote the discharge of thyroid hormone from the thyroid gland. This has led to efforts to attribute deficiency or hyperfunction of the thyroid in man to a deficient or abnormally rapid rate of secretion of thyrotrophic hormone. The hyperthyroidism associated with acromegaly probably is the result of the secretion of excessive amounts of thyrotrophic hormone. On the other hand, thyroid deficiency in man less often seems to depend upon a disturbance of the anterior pituitary, and the clinical value of the thyrotrophic hormone in thyroid disorders is still *sub judice*.

The unit is defined as the daily dose, administered for five days, which causes the thyroid lobes of female guinea-pigs approximately to double their size.

Thyrotrophic hormone prepared from the anterior pituitary gland of the pig raised the metabolic rate in man in health and in cases of pituitary insufficiency, but was without effect in myxoedema.—E. F. Scowen, *Lancet*, ii/1937, 799.

The hormone is ineffective when administered orally, and is completely inactivated in the test-tube by pepsin and trypsin. The possible relationship between clinical hyperthyroidism and alterations in the secretory activity of the anterior lobe as regards the thyrotrophic hormone is still speculative. Recent work seems to indicate that in exophthalmic goitre the level of thyrotrophic hormone is decreased, whereas in myxoedema it is raised. The responsiveness of the patient's thyroid to injected thyrotrophic hormone may become a valuable therapeutic test to determine whether a condition of apparent hypothyroidism is of primary anterior lobe or thyroid origin.—J. B. Collip, *Edinb. med. J.*, 1938, 787.

[P1-87] **Thyroantin** (*Richter, London*). Contains the thyrotrophic principle of the anterior pituitary for intramuscular injection; each ampoule contains 100 Junkmann Schoeller units. For hyperthyroidism, low metabolism, obesity.

[P1-87] **Thyrogan** (*British Drug Houses, London*). Dry ampoules, with ampoules of solvent, containing 50 guinea-pig units of the thyrotrophic hormone of the anterior pituitary. *Dose*.—1 ampoule 2 to 3 times weekly by intramuscular injection.

[P1-87] **Thyrotropin** (*Paines & Byrne, London*). Dry ampoules, with ampoules of solvent, containing 100 guinea-pig units of thyrotrophic hormone from the anterior pituitary gland.

**The Lactogenic Hormone.** The manner in which the anterior pituitary controls the development of the breasts and the secretion of milk is more complex than was at first suspected. The important and probably essential glands of internal secretion are the anterior lobe of the pituitary, the ovaries and the cortex of the suprarenal gland. For the growth and development of the breasts an oestrogen analogous to that obtained from ovarian tissue must be secreted

or injected, but removal of the pituitary gland prevents this development due to oestrogens. A working hypothesis regarding the growth and development of the breasts is as follows: gonadotrophic hormones from the anterior pituitary are essential for the normal secretory activity of the ovaries; ovarian secretions (or placental secretions, or both in pregnant animals) bring about the elaboration of a new anterior pituitary secretion which causes growth and development of the mammary glands. Provided that prelactation development has occurred in the breasts, another anterior pituitary hormone, the lactogenic hormone brings about lactation, but it cannot alone initiate lactation in hypophysectomised animals, the presence of the suprarenal cortical hormone or the suprarenal-cortical-stimulating hormone from the pituitary gland being apparently necessary. It is probable that the maintenance of lactation depends upon additional hormones, including those responsible for the continued development of the breasts.

The lactogenic hormone, for which the names "prolactin" and "galactin" have been suggested, has been isolated as a crystalline substance, which is either a protein or closely related to proteins.

The International Unit for prolactin is defined as the specific activity (based on the response of the crop-gland of pigeons) contained in 0.1 mg. of the standard preparation which is dispensed in tablets containing 100 international units.

Prolactin has been tried clinically with reported success in women whose supply of milk had failed.—*Prescriber*, 1936, 184.

The clinical use of prolactin.—*Endocrinology*, 1934, 18, 18.

In a controlled clinical experiment in which one group of nursing mothers was given a daily injection of 1000 pigeon units (Riddle) of lactogenic hormone and another a daily injection containing no hormone, the group receiving prolactin showed no significant increase of milk secretion over the control group.—H. L. Stewart and J. P. Pratt, *Endocrinology*, 1939, 25, 347.

Of 43 women with deficient milk secretion in the first 8 weeks of lactation satisfactory nursing was induced in three-quarters with prolactin.—M. Kenny and E. King, *Lancet*, ii/1939, 828.

**Physolactin** (*Glaxo Laboratories, London*). Preparation of prolactin, the lactogenic hormone of the anterior pituitary, available in 15 ml. bottles, containing per ml. not less than 60 Riddle-Bates units of activity. Used to stimulate the flow of breast milk in cases of failure of lactation, or deficient secretion. The preparation is given by deep subcutaneous injection into the thigh, the dosage being 5, 5, 2, 2 and 1 ml. on successive days. The effect is usually apparent within 24 to 36 hours of treatment. The product has been used successfully up to the sixth week after parturition.

**The Diabetogenic Factor.** The anterior lobe appears to be the principal division of the pituitary gland concerned in the metabolism of carbohydrates. After removal of the pituitary body the concentration of sugar in the blood may be normal or reduced, sometimes markedly, and usually starvation promptly causes hypoglycemia, which may be so severe as to cause convulsions. These effects result from the absence of a diabetogenic hormone, secreted by the anterior pituitary, which may be viewed as an antagonist of insulin, although there is evidence that the antagonism is indirect and depends upon the support of adequate suprarenal function. The diabetogenic hormone probably prevents the prodigal waste of important carbohydrate reserves which, for



example, are maintained in spite of fasting, and which in a body rendered more sensitive to insulin by removal of the pituitary gland are used up at an abnormally high rate. If the pancreas is removed from an animal the secretion of the anterior lobe of the pituitary is not antagonised by insulin, and may be regarded as an important contribution to changes which threaten life, e.g., the accumulation of acetone bodies. If, however, both glands are removed, the important means of regulating carbohydrate metabolism are lost. A unique derangement of metabolism appears and, depending upon conditions such as the nutritional state before operation, the animal resembles sometimes the diabetic animal and sometimes the animal with pituitary deficiency.

It has also been shown that it is possible to produce an extract which when injected on a number of occasions into intact dogs, will cause a permanent condition of diabetes mellitus. This important observation indicates for the first time the production of diabetes by the injection of an extract of normal tissue. The islets of Langerhans are no longer to be seen in the pancreas of these animals, and the diabetes is characterised by a severe glycosuria, relative resistance to insulin and the absence of ketonuria.

The daily administration of a crude anterior-lobe extract to normal rats for two weeks leads to a rise of the insulin content of the pancreas to nearly twice the normal value. The evidence available permits the assumption that the anterior lobe of the pituitary contains a "pancreatrophic" or "insulin-increasing" substance which is not identical with either the diabetogenic or the growth-promoting principle, but at the present stage it cannot be assumed that the substance is a hormone.—H. P. Marks and F. G. Young, *Lancet*, i/1940, 493.

**Diabetogenic effect.** Some points in connection with this factor are worthy of special note: (1) Preparation and conservation of the extract at low temperature are essential. (2) Individuals of certain species (mouse, rat, and guinea-pig) are almost completely insensitive to diabetogenic extracts effective in dogs. (3) The dog is the best animal in which to demonstrate the effect, but some rabbits and cats respond (25 to 50%). The true diabetogenic activity of extracts should be clearly differentiated from simple hyperglycemic responses occurring within a few hours of the injection of the extract.—J. B. Collip, *Edinb. med. J.*, 1938, 795.

As the result of the daily administration of anterior pituitary extract, two dogs became diabetic and remained so after injections were stopped. The permanent diabetes produced differed from that of depancreatized dogs in that the pituitary dogs appeared to be able to survive without insulin, retaining good vigour, and, in one case, without loss of weight.—F. G. Young, *Lancet*, ii/1937, 372.

**The Suprarenal-Cortical-Stimulating Factor.** Another of the earliest signs of removal of the pituitary body is a very rapid diminution in the size of the suprarenal gland, which is due almost entirely to atrophy of the cortex, the medulla being affected scarcely at all. There is a corresponding loss of activity on the part of the cortex. In some species, particularly birds, the interference with the cortical function is so severe as to cause death. In the duck, for example, it is necessary to inject cortin in order to maintain life after hypophysectomy. The administration of a suitable extract of the anterior pituitary not only restores the cortical function, but may cause enlargement of the cortex so that

the suprarenal glands become larger than any ever encountered in normal animals. The physiological interrelationships of the suprarenal cortex and the anterior lobe of the pituitary are important and numerous but they have been exploited only imperfectly. The suprarenal-cortical-stimulating hormone, for which the terms "adrenotrophic" and "corticotrophic" have been suggested, is probably secreted at an increased rate if there is a cortical deficiency, whereas a change in the opposite direction takes place if abnormally large amounts of suprarenal cortical hormone are present in body fluids. Little is known of the chemistry of this hormone, and the methods proposed for its assay have received no careful quantitative study.

This hormone is present in the primary aqueous extract made at pH 5 from the anterior lobes of cattle, pig, or sheep. Most satisfactory results are obtained by using acetone-defatted and dehydrated desiccated anterior lobes and pre-treating them with several volumes of dilute aqueous alkali at pH 10 for 2 to 4 hours at room temperature, thus destroying in part some of the contaminating posterior lobe principles, and probably by hydrolytic action allowing of better extraction of the active principles subsequently, at pH 5. The filtrate obtained at this pH contains practically all of the thyrotrophic and gonadotrophic hormones. It contains some adrenotrophic hormone, but the iso-electrically precipitated protein and glandular residue contain many times as much of this hormone. It is possible that the adrenotrophic hormone exists in two forms, one present in a readily extractable form, the other firmly attached to protein which can only be extracted in a much more acid medium. It has been found that 80% ethyl alcohol, or 70% acetone at a pH of about 2.5, are the most satisfactory solvents to use at this stage to obtain maximum yields of the protein fraction. The acid-alcohol extract is filtered and the pH adjusted to 7 to 8. The precipitated proteins represent the major part of the growth and adrenotrophic hormones contained in the original tissue. The adrenotrophic substance is the most resistant to boiling of all the anterior lobe principles. Prolactin activity has been observed after boiling for 10 minutes at pH 3 and at pH 8. Growth activity is entirely lost in most cases after 10 minutes' heating at pH 2.—J. B. Collip, *Edinb. med. J.*, 1938, 792.

A principle has been demonstrated in primary extracts of pituitary glands which has a trophic effect upon the so-called "dark cells" of the adrenal medulla of hypophysectomised rats. The principle is active by the mouth.—J. B. Collip, *Canad. med. Ass. J.*, 1940, 2.

(For details of biological tests for the anterior pituitary hormones see Vol. II.)

### Dried Pituitary Preparations.

[P1-57] **Pituitary Body, Dried (entire gland)** of the ox.

*Dose*.—1 to 3 grains (0.06 to 0.2 g.) thrice daily.

Five parts of fresh gland yield about 1 of dried gland.

*Uses*. Has been employed to improve metabolism, to raise arterial tension, to increase diuretic action and to improve appetite. Given in menstrual disorders and in exophthalmic goitre and with thyroid (*q.v.*) in obesity.

**OBESITY**. "I have seen too many instances of greater improvement under the combined (oral) administration of pituitary and thyroid extracts than of the latter by itself to attribute them to mere coincidence."—Sir W. Langdon-Brown, *Brit. med. J.*, ii/1936, 984.

[P1-57] **Pituitary (Anterior Lobe) Substance, Dried.**

*Dose*.—1 to 4 grains (0.06 to 0.25 g.). Much larger doses, up to 60 gr. (4 g.), are often given. 5 parts of fresh substance yield 1 part of dried substance.

**Uses.** Has been thought to exercise a stimulating action upon growth, but for this purpose it should be replaced by standardised extracts of growth hormone. The anterior lobe has been given in certain types of obesity, also in later stages of acromegaly but not earlier stages; also in bronchial asthma.

[P1-57] **Antuitrin** (Parke, Davis, London). 1 ml. ampoules of a solution prepared from the anterior lobe of the pituitary. Dose.—1 ml. hypodermically or intravenously, daily.

[P1-57] **Pitexan** (Paines & Byrne, London). Standardised preparation of anterior pituitary lobe in capsules. Dose.—1 capsule thrice daily before meals, increased to three thrice daily.

[P1-57] **Preloban** (Bayer Products, London). Dry ampoules of whole anterior lobe extract, with ampoules of solvent, containing 25 cockerel testicle maturation units. Also available in pellets for oral administration.

### [P1-57] Pituitary (Posterior Lobe) Substance, Dried.

*Syn.* PITUITARIUM POSTERIUS (*U.S.P. XI*).

Dose.—1 to 4 grains (0.06 to 0.25 g.). *U.S.P. X* average dose  $\frac{1}{2}$  grain. No dose is given in *U.S.P. XI*. 4.5 parts of the fresh substance yield about 1 of dried substance.

**Uses.** Has been used in exophthalmic goitre, acromegaly, intestinal paresis, diabetes insipidus, amenorrhœa and enuresis.

**DIABETES INSIPIDUS.** 7 cases in which nasal administration of powdered posterior lobe controlled the thirst and polyuria, with establishment of "compensation" on the second day. The powder, diluted with lactose, was sniffed up the nose thrice daily, and contained 1000 Vœgtlin units per gramme, the average dose being 15 to 90 units.—F. Mainzer, *Brit. med. J. Epit.*, i/1935, 72.

**PEPTIC ULCER.** Satisfactory clinical results in 67 out of 76 cases of peptic ulcer treated by intranasal insufflation of posterior pituitary powder, the dosage being approximately  $\frac{1}{2}$  gr. given four times daily about 30 minutes after meals and at bedtime. As a rule no symptoms or epigastric tenderness were present after 7 to 21 days of treatment. The improvement was frequently accompanied by a gain in weight, appetite and strength. Should be considered complementary to accepted principles of peptic ulcer management.—Metz and Lackey, *Amer. J. digest. Dis.*, 1940, 27.

[P1-57] **Di-Sipidin** (Paines & Byrne, London). Powdered pituitary posterior lobe extract for insufflation. Dose.—1 gr. sniffed up the nose 2 or 3 times daily. In diabetes insipidus.

[P1-57] **Veinotrope** (Continental Laboratories, London). Mixed gland tablets containing parathyroid, suprarenal, posterior pituitary, ovary or testicular extract, and plant extracts. For varicose veins, hæmorrhoids, venous congestion at the menopause, etc.

### Thymus Gland, Desiccated. (1 part = 5 of fresh gland.)

A yellowish amorphous powder, prepared by desiccating the thymus glands, freed from fat, of healthy calves.

Dose.—*B.P.C.* states 2 to 4 grains (0.12 to 0.25 g.); much larger doses have been given.

Until recently the general opinion was against the inclusion of the thymus amongst the endocrine glands. There is no evidence that its removal produces any appreciable result. The work of Hanson (*U.S.A.*) indicates that extracts of thymus may contain a growth-accelerating factor. The clinical use of thymus gland is still purely empirical. The dried gland substance has been given by mouth in defective nutrition of childhood, Graves' disease, hæmophilia, anæmia, leucocythæmia, and rheumatoid arthritis, but evidence of its value in these conditions is lacking.

The absolute weight of the thymus increases rapidly during the first two years of life, changing little till the seventh year, when it again increases, to fall slightly after the eleventh year. Heavier in the male at birth and for the first four years of life, after which the weight is approximately equal in the two sexes until the eleventh year, when it tends to be absolutely heavier in the female.

**The Biological Effects of Thymus Extract.** Hanson's extract is prepared from thymus glands of 2- to 6-week-old calves by extracting with hot 0.5% hydrochloric acid. 1 ml. of extract equals 0.6 g. of fresh calf thymus.  $\rho H$  is about 5. Golden yellow colour; said to be very stable at room temperature.—L. G. Rountree and J. H. Clarke and A. M. Hanson, *J. Amer. med. Ass.*, ii/1934, 1425.

Of late the claims of the thymus to be regarded as an endocrine structure have been discredited, but now there is a reaction. Hanson's thymus extract has been shown by Rountree and others to accelerate the growth and development of rats and to increase their fertility while hastening the onset of adolescence in the offspring of rats thus treated.—Sir W. Langdon-Brown, *Med. Annu.*, 1936, 459.

The arguments in favour of the presence of an active principle in thymus gland are: (a) Hanson's extract produces acceleration in growth and development which is increased in each succeeding generation; (b) removal of thymus gland from rats results in retardation of growth and development of offspring, even in second generation; (c) this retardation is not apparent in the offspring when the parents have received injections of thymus extract.

For résumé of Hanson's results, see Editorial, *Brit. med. J.*, i/1935, 983.

The thymus gland. A general review.—L. G. Rountree, *J. Amer. med. Ass.*, i/1935, 592.

**Thymocrin Solution** (*Endocrines-Spicer, Watford*). Solution prepared from thymus for intramuscular injection, 1 ml. representing 20 gr. of fresh gland. In certain dermatoses, especially psoriasis. *Dose*.—1 ml. daily or on alternate days. In chronic psoriasis, 1 ml. is given daily for five days a week, and continued for 12 to 16 weeks.

[P1-87] **Thymophysin** (*Camden Chemical Co., London*). A combination of extracts of the thymus gland and of the posterior lobe of the pituitary gland, containing 10 i.u. per ml., and stated to have a more prolonged action than that of pituitary extract alone.

### **Pineal Body. Syn. CONARIUM.**

A small reddish-grey cone-like structure, situated behind the third ventricle of the brain above the superior corpora quadrigemina. Little is known of the functions of the pineal gland; it is suggested that it may contain a substance which antagonises the action of the anterior lobe of the pituitary.

Pineal extract (Hanson) in rats has retarded the rate of growth and accelerated the rate of differentiation, and has hastened the onset of adolescence in the offspring of treated parents. The end result is "dwarfism" associated with sexual precocity and relative macrogenitalism. The injection of succeeding generations of parent rats has resulted in the amplification of these biologic effects in their young.—L. G. Rountree, J. H. Clarke, A. Steinberg and A. M. Hanson, *J. Amer. med. Ass.*, ii/1935, 373.

An extract of pineal glands neutralises the growth-stimulating effect of pituitary.—P. Engel, *Klin. Wschr.*, 1934, 13, 1248.

The chief activity of the pineal is an antagonodotropic effect. The substance having this action can be extracted in slightly alkaline aqueous solution.—P. Engel, *Wien. klin. Wschr.*, 1935, 481.

The injection of preparations of from 1 to 4 beef pineal glands failed to reveal antagonodotropic activity in infantile female rats, and the injection of preparations of from 4 to 9.5 beef pineals failed to reveal oestrogenic activity in adult spayed rats.—N. J. Wade, *Endocrinology*, 1937, 681.

**Epiphysan** (*Richter, London*). Ampoules containing 0.5 g. of fresh pineal gland in 5 ml. *Dose*.—2 to 3 ampoules weekly. Hypersexual conditions.

## PIX LIQUIDA

B.P.

*Syn.* TAR, PIX PINI (U.S.P. XI), PIX ABIETINARUM (P. Helv. V),  
GOUDRON VÉGÉTAL (Fr. Cx.).

*Dose.*—2 to 10 grains (0.12 to 0.6 g.) in a pill with lycopodium, or in perles (2½ grains each).

Is known in commerce as Stockholm tar and is obtained by the distillation of the wood of various species of *Pinus* (Pinaceæ).

*Soluble* in alcohol 90%, ether, chloroform, and fixed and volatile oils.

*Uses.* Internally, wood tar is employed only as an expectorant in chronic bronchitis, usually in the form of a syrup. Externally, it is employed in the form of ointments or lotions in the treatment of chronic skin diseases.

*Aqua Picis* (P. Ned. V). *Syn.* AQUA PICEA, EAU DE GOUDRON. 5% by mixing with pumice. P. Helv. V prepares by heating water with tar 5% and sodium bicarbonate 3%.

*Liquor Picis Lign.* Tar 5, powdered quillaia 10, alcohol 90% to 100. Prepare a tincture of quillaia by percolation and macerate the tar in the tincture for two days at 50°. Cool, filter and make up to 100.

*Pilula Picis Liquidæ.* *Dose.*—1 to 5 grains (0.06 to 0.3 g.). Tar 1, soap 1, compound tragacanth powder ½, powdered liquorice 2½. Useful for coughs and for hæmorrhoids—best freshly made.

*Syrupus Picis Liquidæ* (B.P.C.).

*Dose.*—1 to 2 drachms (4 to 8 ml.).

Tar 0.5% w/v with alcohol 90%, sucrose and water.

[P] *Sirupus Picis cum Codeino* (P. Helv. V).

*Dose.*—½ to 2 drachms (2 to 8 ml.). Codeine 1, tar water 100, glycerin 50, alcohol 95% 10, syrup 839.

*Unguentum Picis Liquidæ* (B.P.C.).

Contains 70% of tar in a basis of beeswax and lard. Useful in psoriasis and chronic dry eczema.

*Unguentum Picis Compositum* (P. Ned. V). *Syn.* RINGWORM OINTMENT. Heat together water 20, tar 16, resin 4, and add with stirring starch 16 mixed with water 30, then Venice turpentine 4, acetic acid 30% 8, and water to 100.

*Unguentum Picis Pini* (U.S.P. XI).

Pine tar 50, yellow wax 15, petroleum 35.

*Oleum Picis* (B.P.C.).

*Dose.*—1 to 5 minims (0.06 to 0.3 ml.).

A reddish-brown empyreumatic oil obtained by the distillation of tar from various species of *Pinus*. On distillation it yields **light oil of tar** or **spirit of tar**, a colourless or pale yellow oil, free from empyreumatic odour. The residue on distillation yields rectified oil of tar (*Oleum Picis Rectificatum*), a light yellow oil, darkening on keeping and having an odour similar to that of the original oil.

*Uses.* Rectified oil of tar is deodorant, antiseptic and parasiticide. It has been employed internally as an intestinal antiseptic, and in the form of an inhalation in hot water for chronic catarrh. Externally it is used in the treatment of eczema and other skin affections.

**Oleum Picis Rectificatum** (U.S.P. XI) is the volatile oil from pine tar rectified by steam distillation. *Average dose.*—3 minims.

**Syrupus Picis Pini** (U.S.P. XI). *Average dose.*—2½ drachms (10 ml.).

Mix rectified oil of tar 1 with water 450 and shake 15 minutes. Set aside 24 hours, filter and dissolve sugar 850 in the filtrate and make up to 1000. [Pi] to 1 gr. of apomorphine hydrochloride may also be added to each dose. Useful in chronic bronchitis and winter cough.

**Ether-Soluble Tar Paste** (Martindale, London). *Syn.* E.S.T.P. An ointment prepared by distilling tar in steam and incorporating the ether-soluble distillate in a zinc and lanolin basis. For infantile eczema, chronic eczema with lichenification, lichen simplex chronicus (Widal) and pruritus ani.

**Tar Dermament** (Parke, Davis, London). A combination of alcohol-soluble phenolic resin with 6% of washed crude coal-tar in the form of a paint for the treatment of skin diseases and to relieve the itching of neuro-dermatitis.

**Taroxide** (Abbott Laboratories, London). Ether-soluble coal-tar distillate 1.5%, powdered zinc oxide 10%, starch 25%, petrolatum 58.5%. Also available containing 5% of coal-tar distillate. Moist eczema.

**Pix Burgundica** (B.P.C.). *Syn.* BURGUNDY PITCH (a misnomer, as it comes from Finland and the Black Forest).

The exudate from *Picea excelsa* (Pinaceæ), occurring as a reddish or yellowish-brown mass. Is a mild counter-irritant, and is used in the manufacture of plasters.

**Emplastrum Picis** (B.P.C.). *Syn.* POOR MAN'S PLASTER. Contains about 50% of Burgundy pitch, with olibanum, colophony, yellow beeswax, olive oil and water.

**Pix Carbonis** (B.P.C.). *Syn.* COAL TAR, PIX LITHANTHRACIS (P. Helv. V), OLEUM LITHANTHRACIS, GOUDRON DE HOUILLE (Fr. Cx.).

The chief constituents of coal tar are benzene,  $C_6H_6$ , and its homologues, isolated by fractional distillation from the light oil (b.p. below  $170^\circ$ ); phenol, cresols and naphthalene,  $C_{10}H_8$ , from the middle (or carbolic) oil (b.p.  $170^\circ$  to  $230^\circ$ ); cresols and their homologues from the heavy oil (b.p.  $230^\circ$  to  $270^\circ$ ); anthracene,  $C_{14}H_{10}$ , from the green oil (b.p.,  $270^\circ$  to  $400^\circ$ ); the residue is pitch. The tar also contains small quantities of basic compounds such as aniline, pyridine, acridine, carbasole, etc., and sulphur compounds such as thiophene,  $C_4H_4S$ .

*Uses.* Coal tar is used for application to the skin in psoriasis, eczema and other skin affections. The liquor is used in lotions and ointments.

**Pix Carbonis Præparata** (B.P.).

Commercial coal tar heated at  $50^\circ$  for one hour.

*Soluble* almost entirely in chloroform and benzene; partly soluble in alcohol 90%; almost insoluble in water.

*Uses.* Infantile eczema has been well treated by purified coal tar and zinc oxide of each 2 parts, corn starch and soft paraffin of each 16 parts. In obstinate cases a tar paint (crude coal tar 1 oz., collodion 1 oz., acetone 1 oz.) may be used. Applied with brush, repeated every two or three days.

**Balneum Picis Carbonis.** *Syn.* BALNEUM BITUMINIS (L.H.).

Solution of coal tar 8 oz., water at  $95^\circ F$ . 30 gallons.

**Collyrium Picis Carbonis** (B.P.C.). Solution of coal tar 0.6% v/v.

**Liquor Picis Carbonis (B.P.).**

A solution made by macerating prepared coal tar 20% and quillaia 10% in 90% alcohol or industrial methylated spirit for seven days and filtering. The quillaia enables the solution to form an emulsion with water.

**Lotio Picis Carbonis Aromatica.**

Coal tar 3 oz., ether 2 oz., alcohol 90% 1 oz. Dissolve, filter and add balsam of Peru 6 dr., salicylic acid  $1\frac{1}{2}$  dr.

**Lotio Picis Carbonis Alkalina (B.P.C.).** Solution of coal tar about 1 in 50, with sodium bicarbonate in water.

**Lot. Picis Alk. (N.I.F.).** Methylated solution of coal tar 1 dr., sodium bicarbonate 30 gr., water to 8 oz.

**Lotio Picis Carbonis et Plumbi (B.P.C.).** Solution of coal tar about 1 in 50 and strong solution of lead subacetate about 1 in 30 in water.

**Pasta Picis Carbonis (B.P.C.).** Coal tar 15 gr., compound paste of zinc oxide to 1 oz.

**Pasta Zinci et Picis Carbonis (C.X.H.).** *Syn.* WHITE'S TAR PASTE. Coal tar 30 gr., zinc oxide 30 gr., starch 180 gr., soft paraffin to 1 oz.

This ointment offers excellent results in the treatment of infantile eczema, especially of the face; the ointment is applied as often as is necessary to keep the face covered. It should not be used if pyogenic infection is present.—F. Wise and J. Wolf, *J. Amer. med. Ass.*, ii/1938, 2106; L. W. Hill, *ibid.*, 2113.

**Pigmentum Picis Carbonis (St. T. H.).** Crude coal tar 10 g., benzene 20 g., acetone 70 g.

**[P1] Unguentum Petrolei Compositum cum Acido Salicylico (St. J. H.).** Solution of coal tar 1 dr., ammoniated mercury 15 gr., salicylic acid 20 gr. paraffin ointment to 1 oz.

**Unguentum Picis Carbonis (B.P.C.).**

Solution of coal tar about  $6\frac{1}{2}\%$  in yellow soft paraffin.

**[P1] Unguentum Picis Carbonis Compositum (B.P.C.).**

Solution of coal tar about  $6\frac{1}{2}\%$  and ammoniated mercury about 3% in yellow soft paraffin.

**Anthrasol (Knoll, London; Savory & Moore, London).** An oily, non-staining tar substitute.

**Liquor Carbonis Detergens (Wright, Layman & Umney, London).**

A preparation of coal tar resembling Liquor Picis Carbonis. Used as a lotion, from 1 dr. to 1 oz. to a pint of distilled water, it forms a yellowish milky emulsion; or, as an ointment, Liquor Carbonis Detergens 1, Unguentum Hydrargyri Nitratis 3, Unguentum Simplex 4. In prurigo and chronic scaly skin diseases.

The following is also useful in eczema: Liquor Carbonis Detergens 2, Liquor Plumbi Subacetatis 2, Zinci Oxidum 4, Glycerinum 4, Aqua 36.

**Oleum Cadinum (B.P., U.S.P. XI, P. Helv. V, Fr. Cx.).** *Syn.* JUNIPER TAR OIL, OLEUM JUNIPERI PYROLIGNEUM.

A dark reddish-brown or nearly black oily liquid obtained by the distillation of the wood of *Juniperus Oxycedrus* (Pinaceæ). This oil is very variable.

**Soluble** 1 in 3 of ether, and in chloroform; partly soluble in cold alcohol 90%, almost completely in hot alcohol 90%; very slightly soluble in water.

**Uses.** Employed in psoriasis, dry eczema and seborrhœic conditions of the scalp. The latter is well treated with soap and water followed by a salicylic lotion, and by oil of cade 1 in 5 of olive oil, gradually increasing the strength till the pure oil is used.

**Oleum Cadini Aceticum.**

Acetic acid 1, cade oil 10. This and the oil itself are used for alopecia.

**Unguentum Olei Cadini (B.P.C.).**

Oil of cade 25% in beeswax and yellow soft paraffin.

**Unguentum Olei Cadini et Sulphuris.**

Oil of cade 10, sulphur 1, soft paraffin 15, hydrous wool fat 15.

**Ung. Sedativ. (N.I.F.).** Calamine 60 gr., zinc oxide 60 gr., oil of cade 15 m., hydrous wool fat 120 gr., yellow soft paraffin to 480 gr.

**Oleum Fagi Pyroligneum. Syn. OIL OF BEECH TAR.**

Used on the Continent as a source of creosote.

**Linimentum Picis (Lassar).**

Beech tar 4, birch tar 3, olive oil 1, alcohol (70%) 1.

**Unguentum Betulæ Compositum (St. G. H.).**

Oil of cade 1 dr., resorcinol 10 gr., ichthammol 10 gr., oil of sweet birch 10 m., lard to 1 oz.

**Oleum Rusci (B.P.C.). Syn. BIRCH TAR OIL, OLEUM BETULÆ ALBÆ, OLEUM BETULÆ PYROLIGNEUM.**

Obtained by the destructive distillation of the wood and bark of *Betula alba*, allowing the distillate to stand, and pouring off the oily upper layer from the residual tar. Occurs as a thick brownish-black liquid. To be distinguished from *Oleum Betulæ* (p. 101).

**Unguentum Rusci Compositum (B.P.C.).**

Contains 8% of birch tar oil with resorcinol, zinc oxide and starch in a wool fat and paraffin basis. For chilblains, eczema, prurigo and psoriasis, and for irritation due to piles.

**Pix Betula (P. Helv. V).** *Syn. BIRCH TAR.* A yellowish-brown oil from *Betula alba* (L.).

**Huile de Bouleau** is obtained by distillation of *Betula alba*.

**Ung. Sedresol (Ferris, Bristol).** A combination of beech tar, zinc oxide and antiseptics. Sedative, antiseptic and healing in eczema, psoriasis, erysipelas, shingles, erythema, seborrhœa, dermatitis, pruritus ani and vulvæ, in inflammations and eruptions of the skin, and in burns and scalds.

**PLUMBUM**

Pb = 207·22.

[P1] "Lead acetates; compounds of lead with acids from fixed oils."

[81] "Lead, compounds of, with acids from fixed oils."

[83] "Lead acetate—in substances containing less than 4 per cent of lead acetate."

"Lead, compounds of,—in machine-spread plasters."

[86] "Lead, compounds of, with acids from fixed oils—specify proportion as the proportion of lead oxide (PbO) that the preparation would be calculated to contain on the assumption that the lead in the poison had been wholly converted into lead oxide."

[P1] **Plumbi Acetas (B.P., U.S.P. XI, P. Helv. V, Fr. Cx.).**

*Syn. SUGAR OF LEAD, SACCHARUM SATURNI.*

$(\text{CH}_3\text{COO})_2\text{Pb} \cdot 3\text{H}_2\text{O} = 379\cdot3$ .

*Dose.*— $\frac{1}{4}$  to 2 grains (0·03 to 0·12 g.).

Colourless crystals or masses efflorescing in warm air.

*Soluble* 1 in less than 2·5 of water, 1 in 30 of alcohol 90%, 1 in 2 of glycerin.



**Incompatible** with carbonates, soluble chlorides, sulphates, tannates, potassium iodide and opium preparations. The *subacetate* is incompatible with acacia mucilage.

**Antidotes.** In *acute poisoning*. Empty stomach by emetic, then give  $\frac{1}{2}$  oz. of magnesium sulphate in water; or use stomach tube with 2 oz. of magnesium sulphate in 2 gallons of water. Demulcent drinks. Hot applications to abdomen, and morphine,  $\frac{1}{2}$  gr. hypodermically, if necessary for pain. Sodium thiosulphate, 5 ml. of 10% solution intravenously, said to be useful.

In cases recognised before the onset of convulsions, fairly large doses of calcium lactate or phosphate are useful with vitamin D to increase its absorption. In cases with convulsions, 20 to 30 ml. of 8% solution of magnesium sulphate subcutaneously or 30 to 50 ml. of 50% dextrose intravenously. Magnesium sulphate by mouth. Later, large doses of calcium gluconate intramuscularly; calcium phosphate and vitamin D for 2 or 3 months. Iron for the *anæmia*.—J. R. Ross and A. Brown, *Canad. pub. Hlth J.*, 1935, 26, 237.

A case of severe lead poisoning with recovery in a woman after the ingestion of 110 gr. of lead acetate taken over a period of a month for purposes of criminal abortion. The patient was first put on a high calcium diet, and given 15 gr. of calcium lactate thrice daily, and when the acute symptoms had subsided was switched to a low calcium intake with parathyroid extract parenterally. —J. N. M. Chalmers and S. L. Tompsett, *Lancet*, i/1938, 994.

**Heavy Metal Antidote.** Dissolve sodium hydroxide 2 g. in 1 l. of water and saturate the solution with hydrogen sulphide. Add the solution to a solution of magnesium sulphate 7.5 g. and sodium bicarbonate 25 g. in 1 l. of water. Cool to 0°, again saturate with hydrogen sulphide and store in rubber-stoppered bottles sealed with paraffin. It is effective against antimony, bismuth, silver, cadmium, cobalt, copper, iron, manganese, mercury, nickel, osmium, lead, thallium and zinc, also against arsenic.—L. Freudweiler, *Schweiz. ApothZtg*, 1937, 75, 25.

**In chronic poisoning.** Formerly the method of treatment was to administer potassium iodide in full doses to dissolve out the lead salts accumulated in the tissues, and these were then eliminated from the circulation by the daily use of magnesium sulphate. This method has now been largely superseded by treatment with large doses of ammonium chloride (90 gr. daily taken in 15 gr. capsules at intervals throughout the day, followed by copious draughts of water) and a diet low in calcium. Parathormone may also be used to mobilise lead and calcium from the bones, but it is not so safe and the results cannot so readily be controlled. (See Whitla's Dict. of Treatment, 8th Edn., 1938.)

Patients suffering from chronic lead poisoning showed clinical improvement when treated with supplements of vitamin C. The constant absorption of lead, as for example by painters, may cause the exhaustion of the vitamin C reserves due to the formation of poorly ionised compounds of lead and vitamin C which are much less toxic than the metal itself. Thus additional amounts of vitamin C are required, and may be obtained by daily doses of 50 mg. of ascorbic acid added to a diet already rich in the natural vitamin.—H. N. Holmes *et al.*, *Science*, 1939, 89, 322.

**DISTRIBUTION AND STORAGE OF LEAD IN THE ORGANISM.** It has been shown that lead is retained indefinitely in the solid portion of the bones. Such lead is harmless, but is held at a point where its liberation would flood the organism with toxic soluble lead. A depleted alkali reserve tends to mobilise the stored lead.—A. S. Minot and J. C. Aub, *J. Pharmacol.*, March 1924, 159.

Lead is absorbed most easily through the respiratory tract, and as little as 1 to 2 mg. daily is likely to produce chronic poisoning.—*J. Amer. med. Ass.*, ii/1925, 2034.

Gastro-intestinal absorption of lead is of less importance than respiratory, since the liver forms a very effective barrier to the passage of lead into the circulation, but lead compounds entering the lungs as fume or dust are absorbed rapidly from the lungs and directly enter the circulation. A concentration of lead in air of 2 mg. in 10 c.m. is the maximum permissible if full health and vigour is to be maintained.—R. E. Lane, *Lancet*, ii/1936, 206.

CIDER. An outbreak of lead colic in Devonshire among cider-drinkers due to lead conducting pipes, used to draw the cider from the cask to the engine. Owing to its greater acidity, cider is a more active solvent of lead than beer.—M. C. N. Jackson and L. N. Jackson, *Lancet*, ii/1932, 717.

SNUFF wrapped in tinfoil caused three cases of chronic poisoning.—J. Uttal, *J. Amer. med. Ass.*, i/1928, 290.

A serious case of chronic lead poisoning due to theatrical grease paint which was found to contain nearly 40% of lead present in the form of a lead oxide or litharge (PbO).—E. L. Bartleman and C. Dukes, *Brit. med. J.*, i/1936, 528.

LEAD IN FOOD. A collection and examination of the information available on the subject is published by G. W. Monier-Williams, Reports on Public Health and Medical Subjects, No. 88, H.M.S.O., per *Analyst*, 1939, 33.

For references to lead poisoning by paint and tetra-ethyl lead see Vol. II.

**Uses.** Both internally and externally (on broken skin) lead salts exert a potent astringent action. They are employed internally in severe diarrhoea, dysentery and catarrhal conditions of the intestines, but careful watch should be kept for toxic effects. Externally lotions are employed for their soothing and astringent properties in skin conditions such as pruritus ani and eczema, and in burns and bruises. Suppositories are employed for rectal hæmorrhage and (with opium) for piles.

[P1] **Glycerinum Plumbi Subacetatis (B.P.C.).**

Prepared by evaporating Liquor Plumbi Subacetatis Fortis and taking up the residue in glycerin.

In chronic eczema glycerin of lead subacetate is useful. It should first be applied diluted 1 part with about 7 of glycerin, or better 1 with 7 of water, and the strength gradually increased; it desiccates the eruption without producing a hard crust. Some uterine affections are well treated with the diluted glycerin.

**Injectio Plumbi (L.H.). (Vaginal).**

Strong solution of lead subacetate 60 m., water to 20 oz.

**Linimentum Boeckii (P. Svec. X).**

Dilute lead subacetate solution 56, talcum 18, starch 18, glycerin 8.

**Liquor Plumbi Subacetatis Dilutus (B.P.).** *Syn.* LIQUOR PLUMBI SUBACETATIS, GOULARD'S LOTION or WATER, LOTIO PLUMBI.

1 of the concentrated solution with water to 80.

For inflamed joints after injury to bruised surfaces, lead lotion (warmed) is useful.

[P1] **Liquor Plumbi Subacetatis Fortis (B.P.).** *Syn.* GOULARD'S EXTRACT.

Prepared by digesting lead monoxide in an aqueous solution of lead acetate. Contains 19 to 21.5% w/w of Pb, and alkalinity corresponding to 10.2 to 11.6% of PbO.

**Lot. Picis Carb. et Plumbi (N.I.F.).** Solution of coal tar (methylated) 2 dr. strong solution of lead subacetate 2 dr., water to 8 oz.

[P1] **Lotio Plumbi cum Opio (B.P.C.).**

Tincture of opium 1 in 20 in dilute solution of lead subacetate.

Although used to a certain extent in this form, opium is said to be entirely devoid of peripheral anæsthetic effects and lead likewise, because the precipitation of proteins is prevented by the intervention of the epithelium.

[P1] **Lot. Plumbi c. Opio (N.I.F.).**

Liquid extract of opium 20 m., strong solution of lead subacetate 4 dr., water to 8 oz.

**Lotio Plumbi Evaporans (B.P.C.).** Strong solution of lead subacetate 1 in 80 in alcohol and water.

**Lot. Plumbi Evap. Conc. (N.I.F.).** Strong solution of lead subacetate  $\frac{1}{2}$  oz., industrial methylated spirit 2 oz., water to 8 oz.

[P1-S1] **Pilulæ Plumbi cum Opio (B.P.C.).** *Dose.*—1 or 2 pills.

Contain lead acetate  $1\frac{1}{2}$  gr., and powdered opium about  $\frac{1}{4}$  gr. (*exempt [D]*).

[P1-S1] **Suppositorium Plumbi cum Opio (B.P.).** *Syn.* SUP-  
POSITORIUM PLUMBI COMPOSITUM.

Unless otherwise stated contains 3 grains (0.2 g.) of lead acetate and 1 grain (0.06 g.) of powdered opium in oil of theobroma *q.s.* to 15 grains (*exempt [D]*).

[P1-S1] **Tabellæ Plumbi cum Opio (B.P.C.).** *Dose.*—1 tablet.

Contain in each lead acetate 3 gr. and powdered opium  $\frac{1}{2}$  gr. (*exempt [D]*). For preparations of similar composition also *exempt [D]* see p. 1141.

**Unguentum Glycerini Plumbi Subacetatis (B.P.C.).**

Glycerin of lead subacetate 1 in 6, in white paraffin ointment.

[P1] **Unguentum Plumbi Acetatis (B.P.C.).**

Lead acetate 4%, in white paraffin ointment.

**Unguentum Plumbi Subacetatis (B.P.C.).**

Strong solution of lead subacetate 1 in 8, in a wool fat and paraffin basis.

[P2-S1] **Plumbi Arsenas.** A white insoluble powder. Used in paste form in horticulture.

**Plumbi Carbonas (B.P.C., P. Helv. V).** *Syn.* WHITE LEAD, CERUSSA (*P. Helv. V, P. Ned. V*).

Composition corresponds approximately to  $2\text{PbCO}_3, \text{Pb(OH)}_2 = 775.7$ .

Heavy white insoluble powder, soluble in dilute acetic and nitric acids. Used as dusting powder for burns and as a 1 to 10% ointment in skin diseases.

**Unguentum Plumbi Carbonatis (B.P.C.).** 10% in white paraffin ointment.

**Paré's Ointment (British Drug Houses, London).** An ointment containing finely powdered lead amalgam for application to malignant ulcers.

**Plumbi Iodidum (B.P.C., Fr. Cx., P. Helv. V).**  $\text{PbI}_2 = 461.1$ .

Yellow crystalline powder. Very slightly soluble in water. Used to reduce swellings and as a 5 to 10% ointment in skin diseases.

**Unguentum Plumbi Iodidum (B.P.C., Fr. Cx.).** 10% in benzoinated lard.

**Plumbi Monoxidum (B.P., P. Helv. V, Fr. Cx.).**  $\text{PbO} = 223.2$ . *Syn.* PLUMBI OXIDUM, MASSICOT, LITHARGE.

Yellowish-red powder or scales soluble in acetic acid and caustic alkalis. To prepare lead plasters and Liqueur Plumbi Subacetatis.

**Minium** (*P. Belg. IV, P. Helv. V*).  $Pb_2O_3 = 685.7$ . *Syn.* RED LEAD.  
Made by heating massicot.

**Colloidal Lead and Colloidal Lead Selenide.** Colloidal lead, either as the metal or in combination, has been employed in the treatment of cancer. Its use was first suggested by W. Blair Bell in 1922 and was based on the abortifacient action of lead due to its toxic action on the cells of the chorionic villi; since these cells somewhat resemble malignant cells in growth, it was argued that the action of lead would be inimical to the growth of cancer cells. Many lead-containing substances, including colloidal lead, colloidal lead phosphate, colloidal lead iodide, and colloidal lead selenide were tried. They were administered intravenously, usually in conjunction with X-ray or radium therapy. The treatment gave rise to considerable discussion among clinical research workers, but owing to the lack of concordant results and the serious toxic effects which were frequently encountered it did not achieve widespread recognition, and has now been largely abandoned.

*For further details as to methods of preparation, dosage, and clinical results, see Vol. I, 21st Edn., pp. 792-794.*

## PODOPHYLLI RESINA

*B.P., U.S.P. XI, Fr. Cx., P. Helv. V.*

*Syn.* PODOPHYLLIN.

**Dose.**— $\frac{1}{4}$  to 1 grain (0.016 to 0.06 g.).

A yellowish powder, or in brownish-grey masses consisting of a mixture of resins obtained either from podophyllum or from Indian podophyllum. It is very irritating to the eyes and requires careful handling.

**Soluble** completely or almost completely in alcohol 90%, insoluble in cold water, partly soluble in hot water but precipitated again on cooling, partly soluble in chloroform, ether and dilute solution of ammonia.

**Uses.** Resin of podophyllum is a potent cholagogue and purgative. It is slow in action, taking from 10 to 12 hours to cause evacuation, and producing several soft stools. It causes severe griping when given alone and is thus usually administered with hyoscyamus or belladonna; moreover, since individual reaction to it varies considerably it is advisable to begin with small doses. It is mainly employed in habitual constipation associated with hepatic insufficiency. For the treatment of gall-stones it may be advantageously combined with calomel in a pill.

[P1-s1] **Pilulæ Podophyllini, Belladonnæ et Nucis Vomicae** (*B.P.C.*).

**Dose.**—1 or 2 pills.

Contain 1 gr. of aloe and  $\frac{1}{4}$  gr. each of resin of podophyllum, dry extract of belladonna and dry extract of nux vomica.

[P1] **Pilulæ Podophyllini Compositæ** (B.P.C.). *Dose*.—1 pill.

Contain resin of podophyllum  $\frac{1}{2}$  gr., mercurous chloride 1 gr. and dry extract of belladonna  $\frac{1}{2}$  gr.

[P1] **Pilulæ Podophyllini et Quininae** (B.P.C.). *Syn.* POORE'S PILLS.

*Dose*.—1 pill. Quinine sulphate 1 gr., resin of podophyllum  $\frac{1}{2}$  gr., dry extract of belladonna  $\frac{1}{2}$  gr., aloe 1 gr. Useful "dinner pills"; must be taken with food.

**Tinctura Podophylli** (B.P.C.).

*Dose*.—5 to 15 minims (0.3 to 1 ml.).

Resin of podophyllum 3.65% in alcohol 90%.

In dose of 2 to 4 drops in tea or coffee, taken night and morning, is useful in sick headache and biliousness, where the bowels and liver are sluggish. Also relieves constipation with clay-coloured motions following diarrhoea of infants; 1 or 2 drops on sugar twice or three times a day.

**Tinctura Podophylli Indici** (B.P. '14) is also made same strength.

**Tinctura Podophylli Ammoniata** (B.P.C.).

*Dose*.—10 to 20 minims (0.6 to 1.2 ml.), diluted, as a purgative and cholagogue. Resin of podophyllum 2% w/v in aromatic spirit of ammonia. Is miscible with water. The sal volatile acts as a corrective.

**Podophyllum** (B.P., U.S.P. XI, Fr. Cx.). *Syn.* MAY APPLE ROOT, AMERICAN MANDRAKE, VEGETABLE MERCURY.

*Dose*.—2 to 10 grains (0.12 to 0.6 g.).

The dried rhizome and roots of *Podophyllum peltatum* (Berberidaceæ) from eastern U.S.A. and Canada. Used mainly in the form of the resin of which it yields from about 2 to 8%. U.S.P. XI requires a minimum of 4%.

**Podophyllum Indicum** (B.P.).

*Dose*.—2 to 10 grains (0.12 to 0.6 g.).

The dried rhizome and roots of *Podophyllum emodi* (Berberidaceæ) from the Himalayas. It yields from 6 to 12% of resin not identical with that from podophyllum.

**Collinsonia** (B.P.C.). The rhizome of *C. canadensis* (Labiatae), known also as stone-root or knob-root, heal-all, hardhack. Has been employed in gravel and other urinary affections. Is an antispasmodic in flatulent, infantile, and biliary colic, and locally in lax conditions of the uvula, pharynx, and vocal cords. *Liquid extract*, 1 in 1, *dose*.—15 to 30 minims.

**Tinctura Collinsoniae** (B.P.C.). *Dose*.— $\frac{1}{2}$  to 1 drachm. 1 in 10.

Has action of podophyllum but does not cause griping.

## POTASSII HYDROXYQUINOLINI SULPHAS

B.P.C.

*Syn. and Prop. Name.* OXYCHINOLINUM SULFURICUM (P. Helv. V), POTASSIUM OXYQUINOLINE SULPHATE, CHINOSOL (*Chinosolfabrik, Hamburg*; *C. Zimmermann, London*).

Consists of a mixture of potassium sulphate and 8-hydroxyquinoline sulphate,  $(C_9H_7(OH)N)_2H_2SO_4 = 388.2$ , containing the equivalent of about 50% of 8-hydroxyquinoline. Chinosol was originally stated to be potassium-oxyquinoline sulphate, but the

content of potassium in the original article of commerce does not agree with theory. Occurs as a light yellow, crystalline powder partially melting at about  $178^{\circ}$ , and giving a strongly acid solution.

**Soluble** in water, sparingly soluble in alcohol, insoluble in ether.

**Uses.** An antiseptic used in skin affections in 1 in 2000 to 1 in 500 solution. Tricophytic conditions of face, arms and wrists have been cured by repeated applications of 1 in 2000 solution. Is an ingredient of some perspiration deodorants and is extensively used in proprietary chemical contraceptives.

**CONTRACEPTIVE USE.** As a few women apparently absorb sufficient quinine to cause sleeplessness and slight digestive disturbances, a suppository of Chinosol in cocoa-butter is recommended by the C.B.C. Med. Research Committee.—*Lancet*, ii/1927, 42.

Chinosol in any medium is not tolerated by a considerable number of women. Its use frequently produces inflammation and discharge, whilst sterility is stated in one instance to have been caused by it. A lactic acid pessary in conjunction with an occlusive pessary found most efficient.—Norman Haire, *Lancet*, ii/1927, 143. See also *ibid.*, *Lancet*, ii/1927, 256, 308 and 360.

**Bircon Tablets** (*London Rubber Company, London*). A foaming tablet said to contain Chinosol, zinc phenolsulphonate, sodium bicarbonate and other suitable antiseptics and deodorants.

**Lomolo** (*Napp, London*). Contraceptive foaming tablets of hydroxyquinoline sulphate, zinc phenolsulphonate and an effervescing base.

**Mil-San** (*Menosine Ltd., London*). A jelly with high viscosity and low surface tension containing boric, acetic, formic, lactic and tartaric acids, aluminium acetate and potassium hydroxyquinoline sulphate in a colloid base. Contraceptive supplied in single application tubes.

**Ortho-Gynol** (*Johnson & Johnson, Slough*). Boric acid, hydroxyquinoline sulphate and glycerin in a water-soluble vegetable gum base. Supplied in individual tubes, each with applicator, or in bulk tube with single applicator.

**Quinolol Compound Ointment** (*Squibb, New York; Savory & Moore, London*). Chlor-hydroxyquinoline 0.5 g., benzoyl peroxide 10 g., aromatic oils 0.24 g., soft paraffin and deodorised wool fat to 100 g. Advocated for cutaneous affections and superficial lesions.

**Chiniofonum** (*B.P. Add. D*). *Syn. and Prop. Names.* PULVIS CHINIOFONI (*U.S.P. XI*), QUINOXYL (*Burroughs Wellcome, London*), YATREN (*Bayer Products, London*).

**Dose.**—1 to 8 grains (0.06 to 0.5 g.); by rectal injection, 15 to 75 grains (1 to 5 g.). *U.S.P. XI* average dose, 15 grains.

Consists of a mixture of approximately 4 parts of 7-iodo-8-hydroxyquinoline-5-sulphonic acid and 1 part of sodium bicarbonate. It contains 28.2 to 29.6% of I and 18 to 22% of  $\text{NaHCO}_3$ , and occurs as a light yellow, odourless powder with a taste at first bitter, subsequently sweetish. *U.S.P. XI* describes it as a mixture of 7-iodo-8-hydroxyquinoline-5-sulphonic acid, sodium bicarbonate and sodium iodohydroxyquinoline suphonate containing 26.5 to 28.9% of I. It is stable in the tropics if kept dry and protected from light.

A mixture of chiniofon 95%, and opium 5%, is *exempt* [D].

**Soluble** 1 in about 25 of water with effervescence; insoluble in alcohol, ether and chloroform. Aqueous solutions are decomposed by boiling.

**Uses.** In acute and chronic amoebic dysentery up to 15 grains may be given 3 or 4 times daily for a week repeated on 2 or 3 days during 2 following weeks; or a daily enema of 200 to 600 ml. of  $\frac{1}{2}$  to 1% solution at a temperature not above 44° has been advised. In acute and the more serious chronic cases combined rectal and oral administration may be adopted.

In mixed amoebic and bacillary types quite contraindicated *per os*—too irritant.—J. Graham Willmore, *Proc. R. Soc. Med.*, Nov., 1928; G. C. Low, *ibid.*

**Enema solutions.** It is convenient to prepare a stock 5% solution by heating four-fifths of the total volume of freshly distilled water required to 60° to 80° (but no higher), adding the chiniofon slowly with frequent stirring and, when effervescence has ceased, adjusting to the required volume with water. Tap water must not be used. Solutions should be freshly prepared every few days.—O. Turner, *Trans. R. Soc. trop. Med. Hyg.*, 1940, 34, 112.

**Neuroyaten (Bayer Products, London).** A combination of autolysates of *B. prodigiosus*, *Staphylococcus aureus*, and *B. pyocyaneus* with Yaten.

Of value in the treatment of disseminated sclerosis. In the majority of 25 cases treated there was either amelioration of symptoms or arrest in hitherto progressive cases. A dose of 0.1 ml. intravenously or 0.4 ml. intramuscularly to commence with.—S. Silverman, *Brit. med. J.*, ii/1935, 1129.

**Yaten-Casein Ampoules** are made for intramuscular and in rare cases intravenous injection. "Weak": Yaten 0.45 g. plus casein 0.38 g.; "strong": Yaten 0.45 g. plus casein 0.75 g. Doses ranging from 1 to 5 ml. are used as non-specific shock therapy in acute and chronic diseases of muscles and joints, in acute and chronic eye inflammations and in broncho-pneumonia.

**Vioform (Ciba, Horsham)** is iodochlorhydroxyquinoline, proposed as a substitute for iodoform. It contains about 40% of I and about 12% of Cl. Almost insoluble in water, sparingly in alcohol, but soluble in hot glacial acetic acid.

**Enterovioform (Ciba, Horsham).** Iodochlorhydroxyquinoline in 0.25 g. tablets to be taken *per os* or crushed and suspended as enema. In amoebic dysentery, 3 tablets being given daily for 10 days and repeated after a week's rest.

**AMOEBIASIS** well treated. Clinical cure (as determined by stool examinations during a follow-up period of 3 to 6 months) in 38 out of 47 unselected cases. A total dose of 15 g. orally in 2 courses of 0.75 g. daily for 10 days, with a week's rest period between, clears the stools of *E. histolytica* in the average case.—N. A. David and co-workers, *J. Amer. med. Ass.*, i/1933, 1660.

Clinically, Vioform compares favourably with carbarsone. Untoward symptoms (which may occur with as little as 4.0 g. of the drug) are severe gastric distress, with nausea, vomiting, colicky pains, diarrhoea, excessive flatulence, with mucus and blood in the stools. When used rectally, severe local irritation results with concentrations as low as 1:500. Vioform should not be administered in retention enemata for this reason.—H. A. Anderson, *J. trop. Med. (Hyg.)*, 1935, 271.

**Carbantren (Ciba, Horsham).** An association of iodochloroxyquinoline-bismuth (10%), pectin (20%) and charcoal (70%) in the form of odourless and tasteless granules. **Dose.**—2 to 3 teaspoonfuls twice daily with meals. For the treatment of enteritis, fermentative dyspepsia, summer diarrhoea, and intestinal conditions with a tendency to hæmorrhage.

## POTASSIUM

K = 39.10.

*Notes on other potassium salts are included under the corresponding acids (see Index).*

*As a war emergency measure an order (S.R. & O. 1941, No. 273) has been made authorising the replacement of certain potassium*

salts by an equal quantity of the corresponding sodium salt in any prescription, unless the contrary is specifically stated. (See p. 1151.)

**Potassii Bicarbonas** (B.P., U.S.P. XI, Fr. Cx., P. Helv. V).  
 $\text{KHCO}_3 = 100.1$ .

*Dose*.—15 to 60 grains (1 to 4 g.).

White powder or crystals soluble 1 in 4 of water, insoluble in alcohol 90%.

*Uses*. Potassium bicarbonate is used as an antacid, as a liquefying expectorant, and as a diuretic. It is valuable in acute catarrhal conditions of the bladder and urethra, and to prevent the formation of urate calculi. It has a considerable reputation in acute and chronic rheumatism, gout, etc., though the rationale of its action is unknown.

[P1] *Mist. Pot. Bicarb. c. Hyosc. (N.I.F.)*. *Syn.* MIST. POT. CIT. c. HYOSC. Potassium bicarbonate 15 gr., potassium citrate 20 gr., liquid extract of hyoscyamus 5 m., water to  $\frac{1}{2}$  oz.

**Potassii Carbonas** (B.P., U.S.P. XI, P. Helv. V, Fr. Cx.).  
 $\text{K}_2\text{CO}_3 = 138.2$ . *Syn.* SALT OF TARTAR.

*Dose*.—2 to 5 grains (0.12 to 0.3 g.).

White deliquescent powder. Soluble 4 in 3 of water; insoluble in alcohol 90%. Contains about 16% of  $\text{H}_2\text{O}$ , corresponding approximately to  $\text{K}_2\text{CO}_3 \cdot \text{H}_2\text{O}$ .

*Uses*. Its properties are similar to those of the bicarbonate, but it is seldom used internally owing to its caustic and irritant action. Externally it has been employed as a lotion in eczema and urticaria (30 grains to 1 pint).

**Potassii Chloras** (B.P., U.S.P. XI, Fr. Cx., P. Helv. V).  
 $\text{KClO}_3 = 122.55$ .

*Dose*.—5 to 10 grains (0.3 to 0.6 g.).

Manufactured by the electrolysis of a hot aqueous solution of potassium chloride. A white powder or crystals with saline taste.

*Soluble* 1 in 16 of water, 1 in 2 of boiling water, 1 in 30 of glycerin, 1 in 152 of alcohol 60%, almost insoluble in alcohol 90%.

*Incompatible* with oxidisable substances, ferrous salts, sugar, nitrites, calomel, hypophosphites, vegetable powders, potassium iodide.

*Antidotes*. Empty stomach by emetic or stomach tube. Give sodium bicarbonate in water freely. Keep patient warm. Stimulants if necessary, e.g., caffeine sodium benzoate, 2 gr. subcutaneously. Blood transfusion.

Less toxic than potassium chloride. Average lethal dose in rats intravenously 1.5 g. per kilo (chloride 0.82 g.).—J. L. Ulrich and V. A. Shternov, *J. Pharmacol.*, Jan., 1929, 8.

A fatal case of poisoning in a man by taking from 30 to 35 g. over a period of three days in mistake for potassium chloride. Death occurred five days after the last dose.—W. J. Cochrane and R. P. Smith, *Canad. med. Ass. J.*, 1940, 23.

Toxic encephalopathy in a child suffering from ulcerative stomatitis treated with a saturated solution of potassium chlorate in a dose of one teaspoonful every three hours. After a week of this treatment, and a total of 7 to 8 g. of the drug, the child began to show signs of cerebral damage. The condition improved slowly, but doubtful if child will be entirely normal.—per *J. Amer. pharm. Ass. (Abstr.)*, 1939, 389.



Prolonged use of products containing potassium chlorate (e.g., mouth-washes, gargles, dentifrices) might result in sufficient absorption of chlorate, particularly when aided by frictional devices, local lesions such as ulcers and pus pockets, and other inflammatory states, to produce injurious effects. The administration of potassium chlorate has been a common practice in physiologic laboratories to produce damage to kidneys. The traditional use of potassium chlorate in oral preparations lacks a rational or scientific basis. A salt action when desired may be obtained with ordinary sodium chloride.—A.P. Richardson, *J. Pharmacol.*, 1937, 60, 101.

The Council on Dental Therapeutics of the A.M.A. will not accept any dentifrice for daily use which contains potassium chlorate. In Austria a dentifrice containing more than 10% of potassium chlorate cannot be sold without a physician's order.—*J. Amer. med. Ass.*, i/1937, 1343.

**Uses.** It is used as a mouth-wash in stomatitis, especially mercurial and ulcerative, and in other foul conditions of the mouth. It is also an effective gargle in pharyngitis and tonsillitis. Its internal use has been condemned owing to the formation of methæmoglobin. It should be given only with care to young children, and never when there is renal disease.

**LARYNGITIS.** After the very acute stage has been passed the following makes a very satisfactory gargle:—potassium chlorate 12 gr., potassium bicarbonate and sodium bicarbonate of each 6 gr., to an ounce of water. For use, the solution is diluted with equal parts of hot water.—F. C. Ormerod, *Med. Pr.*, ii/1939, 70.

**Collunarium Potassii Chloratis Compositum (C.L.T.H.).**

One teaspoonful of a mixture of equal parts of potassium chlorate, borax and sodium bicarbonate (*Pulvis Potassii Chloratis Compositus C.L.T.H.*) to be dissolved in a quarter pint ( $\frac{1}{4}$  tumbler) of tepid water. Half of the solution to be injected with a syringe along the floor of each nostril night and morning. Afterwards blow the nose freely.

**Gargarisma Chlorig (B.P.C.) (N.I.F.).**

A chlorinated solution obtained by dissolving in water the products of the interaction of potassium chlorate and hydrochloric acid. To be used diluted with water.

The taste is improved if made with chloroform water.

**Gargarisma Potassii Chloratis (B.P.C.).**

Potassium chlorate 1 in 40 in water acidified with hydrochloric acid. It contains practically no free chlorine.

**Garg. Pot. Chlor. c. Phenol. (N.I.F.).** Potassium chlorate 2 dr., liquefied phenol 1 dr., trypan blue  $\frac{1}{2}$  gr., glycerin 1 oz., water to 8 oz. Dilute 1 tablespoonful with  $\frac{1}{2}$  pint of warm water.

**Mist. Pot. Chlorat. c. Ferro (N.I.F.).** Potassium chlorate 5 gr., solution of ferric chloride 10 m., glycerin 20 m., water to  $\frac{1}{2}$  oz.

[P2] **Mist. Pot. Chlorat. et Hydrarg. (N.I.F.).** Solution of mercuric chloride 1 dr., potassium chlorate 7 $\frac{1}{2}$  gr., glycerin 20 m., water to  $\frac{1}{2}$  oz.

**Mist. Pot. Chlor. c. Sod. Salicyl. (P.M.H.).** Potassium chlorate 7 $\frac{1}{2}$  gr., sodium salicylate 10 gr., tincture of orange 10 m., water to 1 oz.

**Tabellæ Potassii Chloratis (B.P.C.)** contain 5 gr. (0.3 g.).

Tablets containing potassium chlorate should not be carried carelessly in the pockets, since there is a likelihood of fire from contact with matches or surfaces containing phosphorus compounds.

**Tabellæ Potassii Chloratis et Boracis (B.P.C.)** contain potassium chlorate 3 gr. and borax 2 gr.

**Trochisci Potassii Chloratis (B.P.C.)** contain 3 gr. of potassium chlorate.

**Potassii Hydroxidum (B.P., U.S.P. XI, P. Helv. V, Fr. Cx.).**  
**Syn. POTASSA CAUSTICA.** KOH = 56.1.

[P2] "*Potassium hydroxide.*"

[83] "*Potassium hydroxide—in substances containing less than 12% of potassium hydroxide; accumulators; batteries.*"

[86] "*Potassium hydroxide—specify proportion as the proportion of potassium monoxide ( $K_2O$ ) which the preparation would be calculated to contain on the assumption that the potassium hydroxide in the preparation had been wholly converted into potassium monoxide.*"

[87] *Potassium hydroxide and articles containing it must be labelled "Caution. This substance is caustic."*

Manufactured by the electrolysis of potassium chloride solution. White deliquescent sticks or cakes, containing not less than 85% of total alkali calculated as KOH.

**Soluble** 1 in 1 of water and about 1 in 3 of alcohol 90%; very soluble in boiling dehydrated alcohol.

**Antidotes.** Treat as for poisoning by ammonia, *see* p. 180.

**Uses.** Caustic for nævi and warts. Given occasionally in mixtures as Liquor Potassii Hydroxidi, as an antacid.

**Liquor Potassii Hydroxidi (B.P.).** 5% w/v.

**Dose.**—10 to 30 minims (0.6 to 2 ml.), freely diluted.

[P2] **Pasta Potassæ et Calcis.** *Syn.* VIENNA PASTE. Potassium hydroxide 5, slaked lime 6, made into a paste when required for use, with alcohol or glycerin. Used as an escharotic.

[P2] **Pasta Londinensis** is similar, using sodium hydroxide.

**REMOVAL OF TONSILS.** "London Paste," freshly made from the powder with a little alcohol useful. About 8 weekly applications sufficient.—H. Norman Barnett, *Lancet*, i/1929, 872.

**Potassii Nitris.**  $KNO_2 = 85.10$ .

**Dose.**— $\frac{1}{4}$  to  $1\frac{1}{2}$  grains (0.016 to 0.1 g.).

**Antidotes.** Treat as for poisoning by amyl nitrite, *see* p. 160.

A crystalline deliquescent powder. It is a vasodilator, improves the cerebral circulation, and is given for migraine, asthma and epilepsy.

**Potassa Sulphurata (B.P., U.S.P. XI, Fr. Cx., P. Helv. V).**  
*Syn.* LIVER OF SULPHUR.

Deliquescent masses, yellowish-brown externally, pale liver-brown internally, becoming yellowish on exposure to air, smelling of sulphuretted hydrogen. Used in skin affections, particularly scabies, either in the form of a bath or as ointment.

**Balneum Sulphuratum (B.P.C.).** Contains 8 oz. of sulphurated potash per 30 gallons.

**Balneum Sulphuris (St. M. H.)** contains 10 oz. of sulphurated potash in 30 gallons.

**Sal Aperiens Sulphuratum (B.P.C.).** *Syn.* HARROGATE SALTS.

**Dose.**—1 to 2 drachms (4 to 8 g.).

Sulphurated potash 3% and potassium acid tartrate 15% in exsiccated magnesium sulphate.

**Unguentum Potassæ Sulphuratæ.** Sulphurated potash 1, sodium carbonate 1, lard 8. For ringworm.

**Unguentum Potassii Polysulphidi (B.P.C.).** *Syn.* DANISH OINTMENT, MARCUSSEN'S OINTMENT, LOMHOLT'S OINTMENT. Contains polysulphides of potassium equivalent to  $12\frac{1}{2}\%$  of sulphur with zinc hydroxide and benzaldehyde in a wool fat and paraffin basis.

**TREATMENT OF SCABIES.** After a hot bath and a thorough scrubbing with soft soap and a brush, the skin is dried and the ointment rubbed into every part of the body except the face and scalp. On the following three days the ointment is again rubbed in night and morning without bathing, and on the fourth day a plain bath is taken. All bed-linen and articles of clothing must be disinfected.

A certain cure for scabies or itch.—A. Cannon, *Brit. med. J.*, i/1930, 148. **Kathiolan** (*Ferrosan, Copenhagen; C. Zimmermann, London*). An ointment used for the same purposes as potassium polysulphide ointment.

## PYRETHRUM

(with DERRIS, NICOTINE and STAPHISAGRIA)

**Pyrethri Flos** (*B.P.C., P. Helv. V*). *Syn.* CHRYSANTHÈME INSECTICIDE (*Fr. Cx.*), (DALMATIAN) INSECT FLOWERS.

The dried flower heads of *Chrysanthemum cineræfolium* (Compositæ), containing pyrethrin I (ester of chrysanthemum monocarboxylic acid and the keto-alcohol, pyrethrolone) and pyrethrin II (the ester of the corresponding dicarboxylic acid). The *B.P.C.* requires a minimum of 0.4% of pyrethrin I.

**Uses.** An insecticide and insect repellent. Kerosene extracts of pyrethrum are commonly used in the preparation of fly-sprays and horticultural insecticides. Pyrethrum ointment has been employed in the treatment of scabies.

**SCABIES.** Pyrethrum ointment affords an efficient agent for the treatment of scabies; it is non-irritant, cleanly, and has a pleasant odour. The ointment consists of an absorbent fatty base in which is dissolved the extractive matter of pyrethrum flowers. It contains 0.75% of pyrethrins, hence 100 g. of the ointment represents 83 g. of pyrethrum flowers. The treatment is as follows: All clothing is removed and the bedclothes changed. On the first night the patient remains in a hot bath for 20 minutes and is then soaped all over with liquid soap; he re-enters the bath, rinses off the lather, and dries himself with a rough towel. The ointment is applied over the whole body. On the second night the ointment alone is applied, but on the third the first night's procedure is repeated. In 517 cases the treatment was perfectly satisfactory in from 5 to 7 days.—S. E. Sweitzer and J. W. Tedder, per *Brit. med. J. Epit.*, i/1936, 36.

**DESTRUCTION OF MOSQUITOES IN AIRCRAFT.** An efficient culicide is the following solution, employed as a spray: Petrol 1000 ml., concentrated extract of pyrethrum 5 g., oil of sassafras 5 ml., methyl salicylate 20 ml. The concentrated extract is prepared by extracting powdered pyrethrum flowers with petrol-ether in a Soxhlet apparatus, the extract being then concentrated to the consistency of treacle. The quantity of the spray required is from 4.8 ml. per cubic metre in small spaces to 2.5 ml. per cubic metre in large spaces.—N. M. J. Jitta, per *Bull. Hyg.*, Jan., 1936, 43.

A mixture of 1 part of pyrethrum extract in kerosene (containing 2% of pyrethrins) and 4 parts of carbon tetrachloride (containing no pyrethrins) has been tried. 5 ml. per 1000 cubic feet, with 5 minutes' exposure, killed 100% of exposed *Aedes ægypti*. By ordinary tests this mixture is non-inflammable.—C. L. Williams, *Publ. Hlth Rep.*, Wash., 1935, 1401.

As an anti-malaria measure the spraying of huts, barrack-rooms and tents with pyrethrum extracts of various formulæ is a very useful procedure. A popular formula in India is: paraffin (2nd grade) 124 oz., liquid extract of pyrethrum 2 oz., carbon tetrachloride 4 oz., oil of citronella 8 oz., petrol 22 oz.—*Trans. R. Soc. trop. Med. Hyg.*, 1939, 33, 299.

**Mosquito Larvicide.** A stable stock emulsion suitable for use as a larvicide in fresh waters and waters of less than 5% salinity is prepared by emulsifying a

mixture of kerosene-pyrethrum extract (obtained by treating 2 lb. of pyrethrum flowers with 2 gal. of kerosene), 1 gal. of water and 8 oz. of 40% liquid coconut oil soap. The emulsion mixed with 10 parts of water kills mosquito larvæ but is not injurious to fish, plants or water fowl. The pyrethrum does not remain toxic after 48 hours. An emulsion suitable for use on waters of more than 5% salinity is prepared by adding a mixture of 2 oz. of cresylic acid and 2 gal. of kerosene-pyrethrum extract to a mixture of 1 lb. of powdered skim milk in 1 gal. of water. Diluted with 10 parts of water, this larvicide has no effect on goldfish and water fowl. Both larvicides are equally effective against mosquito pupæ and larvæ when used at a rate of 50 gal. or more per acre.—J. M. Ginsburg, *per Trop. Dis. Bull.*, 1936, 248.

**Tinctura Pyrethri Floris (B.P.C.).** 1 in 4.

Diluted 1 to 10 with water, it is applied to the skin to prevent insect bites.

**Pymosel (Harwood Laboratories, Watford).** Active principles of pyrethrum. In tablets, for oxyuria, ascariis, ankylostoma, etc.; in granules for tenia.

**Pyrethri Radix (B.P.C., Fr. Cx.).** *Syn.* PELLITORY ROOT, SPANISH PELLITORY. Dried root of *Anacyclus Pyrethrum* (Compositæ).

Pyrethrum root has sialagogue properties and is used to promote a flow of saliva in dryness of the mouth and throat. The tincture may be applied on cotton wool, or rubbed on the gums for the relief of toothache.

**Pastilli Pyrethri (B.P.C.)** contain 1 gr. (0.06 g.).

**Tinctura Pyrethri (B.P.C.).** 1 in 5. A useful sialagogue, causing considerable salivary effusion. Must be given with caution to children, as it is powerful in effect.

[P1] **Tinctura Pyrethri Composita.** Tincture of pyrethrum (root) 2, clove oil 1, camphorated chloroform 1. As toothache drops.

**Derris (B.P.C.).** *Syn.* TUBA ROOT, AKER-TUBA.

The dried rhizome of *D. elliptica* and *D. malaccensis* (Leguminosæ), climbing plants indigenous to Malay and the East Indies. Contains up to 10% of a colourless crystalline substance, rotenone,  $C_{23}H_{32}O_6$ , together with the crystalline substances deguelin, tephrosin and toxicarol, and also a toxic substance isomeric with tephrosin. A valuable horticultural and agricultural insecticide. An insecticidal wash effective against a wide range of pests may be made from 1 lb. of powdered root, 4 oz. of soft soap with water to 1 gallon. The powder produces unpleasant symptoms when inhaled, but is probably harmless to human beings and warm-blooded animals.

**SCABIES.** Application 1 or 2% lotion of rotenone resulted in complete cure of every one of 24 cases. In the majority, four applications resulted in complete involution of the lesions in three or four days.—*Brit. med. J.*, ii/1940, 231.

**Derris Dressing for Warble Fly in Cattle.** All cattle are now required to be treated with a derris preparation for the control of the warble fly. The dressing must be used between March 15th and 22nd, and thereafter at intervals of 27 to 32 days until June 30th. The dressing, which must be prepared immediately before use by diluting with water a preparation in powder form containing powdered derris, must contain per gallon either  $1\frac{1}{2}$  oz. of derris resins or  $\frac{1}{2}$  oz. of rotenone, and 4 oz. of soap. The soap may be added at the time of dilution or included in the powdered preparation.

**Sarevan (Evans, Sons, Lescher & Webb, Liverpool).** A non-oily emulsion of rotenone for the treatment of scabies and dermatitis of parasitic origin.

**Nicotina (B.P.C.).**  $C_{10}H_{14}N_2 = 162.1$ .

[P2] "Nicotine; its salts."

[S1] "Alkaloids, the following; their salts, simple or complex:—Nicotine."

[S3] "Alkaloids—Nicotine—in Tobacco."

A colourless, hygroscopic, volatile, liquid alkaloid from tobacco, *Nicotiana Tabacum* (Solanaceæ). The content may be from 0.5 to 5%, combined as malate or citrate. Sp. gr. about 1.01.

**Antidotes.** Empty stomach by emetic, or by stomach tube using dilute tannic acid solution. Give 5 gr. doses tannic acid, repeated if necessary, or medicinal charcoal in water, freely. Keep patient lying down and warm. Stimulants, *e.g.*, brandy  $\frac{1}{2}$  oz. or aromatic spirit of ammonia  $\frac{1}{2}$  dr. in water; strychnine  $\frac{1}{8}$  gr., or caffeine sodium benzoate 2 gr., hypodermically. Artificial respiration and oxygen inhalations may be necessary.

Nicotine poisoning is a temporary respiratory emergency comparable to drowning (or electrical shock) and should be treated as such. Experiments on dogs with nicotine poisoning treated by (a) artificial respiration alone, and (b) artificial respiration with intracardiac injection of adrenaline. Results quoted in detail. It is suggested that prolonged artificial respiration and, when the heart has stopped, intracardiac injection of adrenaline, should be tried in cases of acute nicotine poisoning in the human.—Frank and Thomas, *J. Amer. med. Ass.*, 1/1936, 507.

Nicotine is a powerful poison when applied to the skin. Collapse of a girl in an insecticide factory following the spilling on her overall sleeve of 2 drachms of 95% solution. Saved by emetics and scrubbing the skin with soap and cold water (hot water accelerates absorption).—L. P. Lockhart, *Brit. med. J.*, 1/1933, 247; see also A. M. Aitken, *ibid.*, 341.

Accidental poisoning of an American florist by spilling on the clothes an insecticide containing 40% of free nicotine. Nausea, vomiting, sweating and dyspnoea. Symptoms cleared up in 3 weeks.—J. M. Faulkner, *J. Amer. med. Ass.*, 1/1933, 1664.

A boy of 5 became unconscious and vomited continually immediately after an enema consisting of 60 ml. of strong tobacco juice in 1000 ml. of water, which was given for threadworms. Recovery took place after three doses of sodium benzoate and copious enemas to eliminate the nicotine.—H. W. Willis, *J. Pediat.*, 1937, 65.

**Uses.** Is practically never used in medicine, but has been suggested for use in post-encephalitic parkinsonism. Nicotine is used as a horticultural insecticide either as vapour or as a spray. For vaporisation 1 oz. is sufficient for 2000 to 8000 cu. ft. As a spray  $\frac{3}{4}$  to 1 oz. of nicotine with  $\frac{1}{2}$  to 1 lb. of soft soap is used in 10 gallons of water.

POST-ENCEPHALITIC PARKINSONISM treated by nicotine. Cases which may benefit are those where voluntary muscular control is intact, but movement is hampered by excessive plastic tone. Nicotine base is used. Signs of intolerance are nausea, fainting, tachypnoea, and are watched for. Patient is kept in bed. Initial dose  $\frac{1}{10}$  grain *ter die*. If no appreciable change in pulse chart the dose was increased to  $\frac{1}{5}$  or  $\frac{1}{4}$  grain *ter die*. Immediate results indisputable.—H. Moll, *Brit. med. J.*, 1/1926, 1079.

[P2-81] **Nicotinæ Sulphas.** A water-soluble salt used in solution as an insecticide in horticulture and as a dressing for animals.

**Staphisagria (B.P.C., Fr. Cx.). Syn. STAVESACRE SEEDS.**

[P1] "*Alkaloids, the following; their salts, simple or complex:—Stavesacre, alkaloids of.*"

[81] "*Alkaloids, the following; their salts, simple or complex:—Stavesacre, alkaloids of, except substances containing less than 0.2% of the alkaloids of stavesacre.*"

[83] "*Alkaloids—Stavesacre, alkaloids of,—in soaps; ointments; lotions for external use.*"

EE\*

[86] "*Alkaloids—Stavesacre, alkaloids of,—specify proportion as the proportion of any one alkaloid of stavesacre that the preparation would be calculated to contain on the assumption that all the alkaloids of stavesacre in the preparation were that alkaloid.*"

**Antidotes.** Give medicinal charcoal stirred up in water, then follow this with an emetic or the use of the stomach tube. Keep patient lying down and quiet.

The seeds of *Delphinium Staphisagria* (Ranunculacæ), containing about 30% of oil and 1% of alkaloids, the most important of which is delphinine, which resembles aconitine in its action.

*Staphisagria* is used chiefly in the form of lotion and ointment to destroy pediculi.

**Lotio Staphisagrie** (B.P.C.). *Syn.* NURSERY HAIR LOTION.

A perfumed decoction of *staphisagria* in dilute acetic acid with alcohol, glycerin and water.

**Unguentum Staphisagrie** (B.P.C.). A mixture of benzoinated lard and yellow beeswax in which *staphisagria* has been digested.

## PYROGALLOL

B.P.C., U.S.P. XI, P. Ned. V, P. Helv. V, Fr. Cx.

$C_6H_3(OH)_3 = 126.0$ .

*Syn.* PYROGALLIC ACID, 1 : 2 : 3-TRIHYDROXYBENZENE.

In light, small, white, odourless crystals, with m.p.  $129^\circ$  to  $135^\circ$ , producing a sensation of coolness on the tongue. Is obtained by heating gallic acid. Alkaline solutions absorb oxygen rapidly.

**Soluble** 1 in 2 of water, about 1 in 1 of alcohol 90% and 1 in 10 of melted lard.

**Uses.** Pyrogallol is not used internally, since it exerts a toxic action on the blood, causing methæmoglobinuria and jaundice. Externally, it is used, similarly to chrysarobin, in psoriasis, lupus vulgaris, ringworm and other parasitic skin diseases, but it is not suitable for application over large areas or denuded surfaces, owing to the possibility of toxic effects from absorption. Jarisch's ointment, which is composed of 60 gr. of pyrogallol in an ounce of lard, is sometimes used in chronic eczema and in phagedenic chancres. Pyrogallol has the disadvantage of staining the skin and hair black. Stains on the skin are removed by ammonium persulphate. It is used as an ingredient of hair dyes and as a developer in photography.

Fatal poisoning following treatment of a universal psoriasis with ointment containing pyrogallol. Patient collapsed 5 minutes after covering about two-thirds of body with ointment. Estimated absorption of about 10 g. of pyrogallol. —*per J. Amer. med. Ass.*, ii/1925, 555.

**LUPUS VULGARIS.** Pyrogallol is the most successful caustic as it has an elective caustic effect on tuberculous granulation tissue. Best employed as: soft paraffin 11, pyrogallol 3, salicylic acid 3, resorcinol 3. The ointment is smeared on a piece of lint, cut to fit the plaque to be treated, and fastened by a bandage. The dressing is changed night and morning, as much destroyed tissue as possible being removed each time. Treatment is rather painful and only tolerated for a few days at a time, when it is replaced by an indifferent soft ointment or a compress of 0.2% resorcinol solution. Valuable in dealing with

the verrucose form of lupus as a preliminary to light treatment.—*Brit. med. J.*, ii/1934, 291.

**SYPHILITIC ULCERATIONS**, resistant to usual treatment, well treated with pyrogallol ointment—2% for 2 days, 10% for 2 days, 20% for 2 days, and 30% for 8 days. The urine has to be controlled (black coloration with overdoses), undermined edges removed, and surrounding tissues protected with zinc paste.—*J. Amer. med. Ass.*, ii/1925, 314.

**Unguentum Pyrogallolis (B.P.C.).** *Syn.* UNGUENTUM ACIDI PYROGALLICI. 12½% in white soft paraffin.

**Unguentum Pyrogallolis Compositum (B.P.C.).** *Syn.* UNGUENTUM ACIDI PYROGALLICI COMPOSITUM, UNNA'S COMPOUND PYROGALLOL OINTMENT. Pyrogallol 5%, ichthammol 5%, salicylic acid 2% in yellow soft paraffin.

**Acidum Pyrogallicum Oxidatum.** *Syn.* OXIDISED PYROGALLOL. A brownish insoluble powder prepared by the action of air and ammonia on pyrogallol. 3 to 10% ointment for skin affections.

**Hydroquinone.** *Syn.* QUINOL, HYDROCHINON.  $C_6H_4(OH)_2$  1 : 4 = 110.0. *Dose.*—½ to 5 grains. An isomeric of resorcinol.

A white powder soluble 1 in 20 of water and 1 in 4 of alcohol. It possesses stronger antiseptic and antipyretic properties than resorcinol. Is used as a photographic developer.

**Eugallol (Knoll, London).** Pyrogallol monacetate, a yellowish syrupy liquid used either undiluted or diluted with acetone for local application in psoriasis and eczema.

**Lenigallol** is pyrogallol triacetate, a white powder used with zinc paste in acute and chronic eczema.

## PYROXYLINUM

*B.P., U.S.P. XI, Fr. Cx.*

*Syn.* COLLOXILINA (*F.E. VIII*), COLLOXYLINUM (*P. Helv. V*), CELLOIDINE.

Prepared by the action of nitric and sulphuric acids on cotton. It has approximately the composition of a cellulose tetranitrate.  $C_{12}H_{16}O_6(ONO_2)_4$ . *P. Helv. V* describes it as a mixture of the di- and tri-nitrates.

**Soluble** freely in methyl alcohol, acetone, amyl acetate, glacial acetic acid and in ether mixed with an equal volume of either ethyl or methyl alcohol.

In making gun-cotton, cellulose hexanitrate,  $C_{12}H_{14}O_4(ONO_2)_6$ , the mixture of acids contains a larger proportion of nitric acid and the time of action is longer. This body is insoluble in a mixture of alcohol and ether.

**Collodium Acetonum (B.P.C.).** Pyroxylin 1 in 20 with oil of clove and amyl acetate in benzene and acetone.

A collodion giving a perfectly plasticised adherent film is produced from the following:—Pyroxylin 1, castor oil 0.5, Cellosolve 2, acetone to 20. The use of medicated collodions is condemned on the ground that an efficient film encloses the medicament and so inhibits any therapeutic action.—H. Berry and L. G. Goodwin, *Quart. J. Pharm.*, 1937, 23.

**Collodium Flexile (B.P.).** *Syn.* COLLODION.

Pyroxylin 2% with colophony and castor oil in alcohol 90% (or industrial methylated spirit) and ether. *Fr. Cx.* has pyroxylin 5,

95% alcohol 20, ether 75 (all by weight); *U.S.P. XI* has 4, 25 and 75, *P. Dan.* 4, 84 and 12, and *P. Helv. V* 4, 66 and 30, respectively.

**Collodium Flexile** (*U.S.P. XI*).

Collodion with 2% of camphor and 3% of castor oil.

**Collodium Elasticum** is collodion with castor oil 5% (*Fr. Cx.*), 3% (*P. Helv. V*), 2% (*P. Austr.* and *P. Ned. V*), or 1% (*P. Dan.*).

**Collodium Simplex** (*B.P.C.*). Pyroxylin, about 1 in 50, in ether and alcohol 90%.

**Celluloid.** Made by dissolving pyroxylin 50 in a solution of camphor 25 in ether 100 and manipulating the mass until it has become plastic. It is then dried. Colours may be incorporated. It is supplied in thin sheets and, being light, rigid and washable, is useful in surgery for splinting; it is rendered plastic by rolling up and macerating in hot spirit for a few minutes; it may then be wrapped round the limb with a layer of wool outside and quickly sets. *N.B.* Very inflammable.

**Soluble** in acetone and in amyl acetate, but the film resulting in the first case is liable to be opaque. Mixtures of these solvents are frequently used. A collodion can be readily made strength 1 in 20 using equal parts of the solvents. (The celluloid should be shredded.)

**"Non-inflammable" Celluloid** is cellulose acetate. It is not actually unburnable, but is as safe as paper. It burns slowly without the evolution of dangerous gases.

## QUINIDINE

(with CINCHONIDINE and CINCHONINE)

**Quinidina** (*B.P.C.*).  $C_{20}H_{24}O_2N_2 \cdot 2H_2O = 360 \cdot 2$ .

**Dose.**—3 to 10 grains (0.2 to 0.6 g.).

White amorphous powder or acicular crystals, m.p. when anhydrous  $168^\circ$ . It usually contains 20 to 30% of the closely related alkaloid, hydroquinidine.

**Soluble** 1 in 2200 of water, 1 in 750 of boiling water, 1 in 17 of alcohol 90%, 1 in 70 of ether. The anhydrous alkaloid is soluble 1 in 1.6 of chloroform.

Its solution in sulphuric acid has a blue fluorescence, as in the case of quinine, and it gives a similar thalleioquin reaction. It differs from quinine in m.p., and its acid tartrate and the hydriodide are only slightly soluble.

**Uses.** Quinidine and its salts are generally considered to be as useful as quinine in malaria, especially the benign tertian form, but they are more depressant to the heart. The salts, chiefly the sulphate, are given in auricular fibrillation.

**Quinidinæ Hydrochloridum** (*P. Ital. V*).  $C_{20}H_{24}O_2N_2 \cdot HCl \cdot H_2O = 378 \cdot 7$ . Colourless silky crystals, soluble 1 in 60 in water.

**Quinidinæ Hydrochloridum Acidum.**  $C_{20}H_{24}O_2N_2 \cdot 2HCl \cdot H_2O = 415 \cdot 1$ . Colourless crystals, soluble 1 in 4 of water.

**Quinidinæ Sulphas** (*B.P.*, *U.S.P. XI*, *P. Ned. V*, *Fr. Cx.*, *P. Belg. IV*, *P. Helv. V*).  $(C_{20}H_{24}O_2N_2)_2 \cdot H_2SO_4 \cdot 2H_2O = 782 \cdot 5$ .

**Dose.**—3 to 10 grains (0.2 to 0.6 g.). *U.S.P. XI* average dose 3 grains 4 times a day.

Occurs as needle crystals, darkening on exposure to light.

**Soluble** 1 in about 90 of water, 1 in 10 of alcohol 90%, and 1 in 15 of chloroform.



**Uses.** In addition to its efficacy in malaria, quinidine may be employed in all forms of fever, and wherever quinine has been used.

The main use of quinidine sulphate is in the treatment of persistent auricular fibrillation. It has a specific depressant effect on the muscle of the auricle, prolonging the refractory period of the muscle and thus tending to render it incapable of maintaining the circus movement of fibrillation and replacing it by normal sinus rhythm. Treatment with quinidine is preceded by rest in bed and a full course of digitalis to relieve the heart failure. The susceptibility of the patient is first tested by a preliminary dose of 0.2 g., followed in two or three hours by a further 0.2 g. If there are no bad effects within twelve hours this is followed by the regular administration of 0.4 g. three to five times a day. If no benefit follows within three days, the treatment is considered unsuccessful and administration stopped. The best results are obtained in cases of recent development and the treatment is contraindicated where the myocardium is severely damaged. Quinidine sulphate is also of value in auricular flutter, as an alternative to digitalis, and in paroxysmal tachycardia.

In susceptible persons quinidine may produce untoward symptoms such as headache, nausea, dizziness, palpitations, etc.

The after-results of treatment with quinidine have been followed in two series of patients, one first treated in 1923-8 and the other in 1929-34; almost all have been followed up to December, 1934, or until fibrillation recurred. Quinidine restored normal rhythm in 64% of 135 cases. In 34% it is still maintained after an average period of nearly 4 years. In 30% it was restored, but fibrillation recurred after an average period of two years. In 36% quinidine failed to restore normal rhythm, or did so for such a short time that it was of no practical importance. Of the earlier series, 25% still maintain normal rhythm after nine years, and 39% of the later series after two years. Quinidine is therefore an effective and often a lasting treatment for auricular fibrillation; its success depends on the careful selection of suitable patients. The ordinary patient seen in hospital is quite unsuitable, the risk is too great, and if fibrillation is arrested it generally returns too soon. Satisfactory results are obtained by paying attention to three main criteria: the absence of congestive failure, of a greatly enlarged heart, or of a long history of fibrillation.—M. Campbell and F. W. Gordon, *Quart. J. Med.*, April, 1936, 224.

It is undesirable to attempt to restore a normal rhythm in established fibrillation by quinidine when (1) there has been any evidence of emboli, (2) there is severe valvular disease, (3) the heart, by an X-ray, is found to be grossly enlarged, and (4) there has been previous congestive heart failure.—A. H. Gosse, *Practitioner*, i/1938, 343.

There is evidence that quinidine and strychnine sulphate have a synergistic action. Normal cardiac rhythm was re-established in 33 out of 41 cases for periods varying from 4 months to two years, by the administration of 5 gr. of quinidine sulphate every three hours and  $\frac{3}{16}$  or  $\frac{1}{10}$  gr. of strychnine sulphate three times daily.—H. L. Smith and E. W. Boland, *J. Amer. med. Ass.*, ii/1939, 1017.

**HYPERTHYROIDISM.** For the cardiac complications of hyperthyroidism quinidine sulphate is considered superior to digitalis.—*Prescriber*, 1927, 172.

**MALARIA.** Observations on the treatment of malaria in 1047 cases, from 1930 to 1934, in Louisiana. Treatment consisted in the administration of quinidine sulphate in 2 10-grain doses for 2 days, night and morning, and 1 10-grain dose at night for 3 more days. The course is repeated only if there is a clinical relapse or the blood smear becomes positive. This course has been found effective in curing about 60% of malignant tertian and 75% tertian malaria; it relieves the acute symptoms of both quickly, is safe to use in cases of pregnancy, and may be tried in hæmaturia and in cases of quinine idiosyncrasy.—J. P. Sanders, *Amer. J. trop. Med.*, 1935, 651

**PAROXYSMAL TACHYCARDIA.** Digitalis rarely appears to have any beneficial effects in paroxysmal tachycardia. Quinidine sulphate is the drug of choice, but it does not uniformly give the desired results. It often diminishes the frequency and the duration of the attacks and occasionally causes their cessation. The drug must be given for long periods, and is therefore undesirable when the paroxysms occur only rarely. The dosage must be individualised, the average dose being between 16 and 20 gr. daily.—F. A. Willius, *Proc. Mayo Clin.*, 1935, 763.

Quinidine sulphate the only therapeutic measure and successful in many cases. Dosage high—as much as 120 gr. daily.—M. B. Strauss, *per Med. Annu.*, 1931, 51.

**Tabellæ Quinidinæ Sulphatis** (*B.P.C.*) contain 3 gr. (0.2 g.).

**Quinicardine** (*Nativelle, Paris; Wilcox, Jozeau, London*). Quinidine sulphate in gelatin-coated tablets containing 0.2 g.

**Quinidinæ Sulphas Acidus.**  $C_{19}H_{21}O_2N_2 \cdot H_2SO_4 \cdot 4H_2O = 494.3$ .

Colourless crystals, soluble 1 in 8 in water.

**Cinchonidina.**  $C_{19}H_{22}ON_2 = 294.2$ .

In short, colourless prisms or leaflets, with m.p.  $202.5^\circ$ . Soluble about 1 in 4000 of water, and about 1 in 20 of alcohol. It does not give the thalleioquin reaction, and its solution in sulphuric acid is not fluorescent. Closely resembles quinine in its action.

**Uses.** Cinchonidine and its salts are less efficacious in the treatment of malaria than quinine or quinidine, and their administration is apt to give rise to epileptiform convulsions. The sulphate is said to be of value, in frequently repeated doses of 5 gr., in rheumatism and neuralgia. The salicylate has been similarly employed, and has also been given for the prevention and treatment of influenza.

**Cinchonidinæ Dihydrochloridum.** *Syn.* CINCHONIDINÆ HYDROCHLORIDUM ACIDUM.  $C_{19}H_{21}ON_2 \cdot 2HCl = 367.1$ .

*Dose.*—1 to 8 grains (0.06 to 0.5 g.).

Crystals readily soluble in water. Convenient for preparing solutions for injection.

**Cinchonidinæ Hydrochloridum.**  $C_{19}H_{21}ON_2 \cdot HCl \cdot H_2O = 348.7$ .

*Dose.*—1 to 10 grains (0.06 to 0.6 g.).

Colourless crystals, soluble 1 in 30 in water.

**Cinchonidinæ Salicylas.**  $C_{19}H_{21}ON_2 \cdot C_6H_4(OH)COOH = 432.2$ .

*Dose.*—1 to 10 grains (0.06 to 0.6 g.).

**Cinchonidinæ Sulphas** (*B.P.C.*).  $(C_{19}H_{21}ON_2)_2 \cdot H_2SO_4 \cdot 7H_2O = 812.6$ .

*Dose.*—1 to 10 grains (0.06 to 0.6 g.).

In silky white needles from mother liquor of quinine sulphate.

**Soluble** 1 in 60 of alcohol, 1 in 100 of water (more so with a little acid).

**Cinchonina.**  $C_{19}H_{22}ON_2 = 294.2$ .

*Dose.*—1 to 10 grains (0.06 to 0.6 g.).

White crystals, tasteless at first, becoming bitter. Soluble 1 in 150 of alcohol 90%, and 1 in 500 of ether; almost insoluble in water (about 1 in 4000).

**Uses.** Cinchonine and its salts have a similar anti-malarial and anti-periodic action to quinine, but, like cinchonidine, they may cause convulsions when given in large doses. The salt most frequently employed is the dihydrochloride, which is given intramuscularly in malarial relapses and the treatment of malignant tertian malaria, especially in patients in whom quinine causes sickness. It should be remembered that since it is more rapidly absorbed than quinine, large doses given intramuscularly may cause cinchonism.

**Cinchoninae Dihydrochloridum.** *Syn.* CINCHONINE ACID HYDROCHLORIDE.  $C_{19}H_{22}ON_2 \cdot 2HCl = 367.1$ .

*Dose.*—5 to 15 grains (0.3 to 1 g.) by intramuscular injection.

White crystalline powder. Soluble 1 in 0.6 of water, 1 in 6 of alcohol and 1 in 115 of chloroform.

**Cinchoninae Hydrochloridum** (*B.P.C.*).  $C_{19}H_{22}ON_2 \cdot HCl \cdot 2H_2O = 366.7$ .

*Dose.*—1 to 10 grains (0.06 to 0.6 g.), or more.

In white acicular crystals. Soluble 1 in 20 of water and 1 in 2 of alcohol 90% and 1 in 300 of ether.

**Cinchoninae Sulphas.** ( $C_{19}H_{22}ON_2$ ) $_2 \cdot H_2SO_4 \cdot 2H_2O = 722.5$ .

*Dose.*—1 to 10 grains or more.

In hard, colourless, short rhombic prisms with a vitreous lustre. Soluble 1 in 70 of cold water, 1 in 10 of alcohol 90%.

## QUININA

*B.P.C., Fr. Cx., U.S.P. XI, F.E. VIII.*

$C_{20}H_{24}O_2N_2 \cdot 3H_2O = 378.3$ . *P. Ned. V* is anhydrous.

*Dose.*—1 to 10 grains (0.06 to 0.6 g.). *U.S.P. XI* average dose 15 grains.

A white, minutely crystalline, flaky powder. Loses 1 molecule of water at ordinary temperatures. When anhydrous has m.p.  $174^\circ$ .

**Soluble.** Slightly, 1 in about 1500, in water, 1 in 4 of ether, about 1 in 1 of alcohol 90%, and 1 in 3 of chloroform. Its solution in dilute sulphuric acid is fluorescent, lævorotatory, and gives, with bromine water and ammonia, a green colour due to thalleioquin.

**Toxic Effects.** The larger therapeutic doses of quinine may give rise to a number of toxic effects (cinchonism). These include ringing in the ears with partial deafness, headache, giddiness, epistaxis and often skin rashes. In susceptible patients these symptoms may follow quite small doses. Very large doses result in deafness and blindness, with death from failure of the heart and respiration.

Death from 48 5-grain quinine bisulphate tablets.—H. M. Raven, *Brit. med. J.*, ii/1927, 59.

Fatal poisoning in child of 2½ following ingestion of 26 5-grain tablets (sugar coated) of quinine sulphate.—S. G. Willmott, *Lancet*, ii/1931, 1133.

Quinine is often used in Greece for purposes of suicide. Doses of 10 g. may not give rise to serious intoxication, but doses of 20 g. and more have often proved fatal.—per *Brit. med. J.*, i/1935, 1130.

Death of a woman following the taking of 16 quinine pills, containing a total of 6.08 g. of quinine sulphate, to procure abortion.—C. K. Vartan and J. Discombe, *Brit. med. J.*, i/1940, 525.

**Uses.** Internally is a bitter stomachic useful in atonic dyspepsia and as a tonic in convalescence and debility. It was formerly used as an antipyretic in fevers, its action in reducing temperature being due to diminished heat production; it has largely been replaced for this purpose by the synthetic antipyretics. It is also given in neuralgia, catarrh and hay-fever. Externally, a paste of quinine in a non-greasy base is of value for preventing burns due to ultraviolet radiation. Aqueous solutions of 0.5 to 1.5% of

soluble salt are used in eye lotions for the treatment of corneal ulcerations, and the 1% solution is useful as a spray in hay-fever.

Pessaries containing 3 gr. of the hydrochloride in oil of theobroma basis are used as a contraceptive.

Moderate doses of quinine stimulate, and high doses depress the contractions and tone of the uterus, the stimulant action increasing with the excitability of the uterus in the later stages of pregnancy, and it may be used clinically to intensify weak labour pains. A dose of 5 gr. daily during the last three or four weeks of pregnancy is said to act both as a general and a uterine tonic, and has been advocated as a preventive of uterine inertia. Pregnancy in malaria is not now regarded as a contraindication to the use of quinine.

Quinine is specific in the treatment of malaria, being particularly effective against the organism when spores are being formed. It should therefore be administered in a dose of 20 to 30 gr. about 3 hours before an attack is due, so that the concentration in the blood shall be a maximum when the spores are liberated, at which stage fever develops. Opinions differ as to its efficacy as a prophylactic against malaria, but it is now generally believed to protect at least a fair proportion of cases if taken in adequate dosage, e.g., 10 gr. daily.

**DYSTONIA.** Dystonia markedly improves under quinine therapy, employing doses of 15 to 30 gr. a day of quinine sulphate (in 5 gr. tablets). The treatment is of benefit even in cases of so-called spasmodic torticollis, or torsion spasm.—G. B. Hassin, *J. Amer. med. Ass.*, ii/1939, 12.

**LABOUR.** "MEDICINAL INDUCTION" (*Castor Oil and Quinine*). 2 oz. of castor oil is given and an hour afterwards  $\frac{1}{2}$  oz. of a mixture containing quinine sulphate 10 gr., dilute sulphuric acid 10 m., glycerin 20 m., spirit of chloroform 5 m., and water to  $\frac{1}{2}$  oz. 1 hour after, a simple enema is given. 2 hours later another dose of the mixture, also 3 hours later and again after 4 hours, the total amount of quinine given being 40 gr. Greater percentage of successes than with pituitary (posterior lobe) extract. Less danger with pituitary extract when preceded by quinine course. Quinine is definitely able to act upon a closed cervix.—K. V. Bailey, *Brit. med. J.*, i/1926, 18; *Lancet*, i/1926, 282.

In normal labour a small dose for 3 weeks prior to the date. Quinine sulphate  $1\frac{1}{2}$  gr., dilute nitrohydrochloric acid 3 m., Syrup. Aurant.  $\frac{1}{2}$  dr., water to 2 dr. *Dose*.—2 drachms with water thrice daily before meals. Two 8-oz. bottles will carry the patient over the 3 weeks.—D. A. Mitchell, *Brit. med. J.*, i/1930, 144.

By giving not more than 5 gr. a day in divided doses, commencing several weeks before the calculated date of parturition, labour is made shorter and easier, there is improved uterine tone (with no complications of irregular contraction), a definite diminution in susceptibility to infection, improvement of general health and more satisfactory puerperium.—W. M. Hewetson, *Brit. med. J.*, ii/1933, 170. Universally good results.—D. J. Gair Johnston, *ibid.*, 266. Value confirmed.—V. B. Green-Armytage, *ibid.*, 397.

In a series of 100 cases, quinine given in single nightly doses of 5 gr. in the last weeks of gestation, acted as a general tonic and stimulant, and the patients felt well and were often improved. No evidence of foetal toxicity or increased foetal morbidity, and little risk of premature labour. The effect on duration of labour is doubtful. Clinically the pains seem improved, but compared with a control series there was no significant difference. Inertia not eliminated.—F. W. Buddie, *Brit. med. J.*, i/1934, 1159; see also D. A. Mitchell, *ibid.*, ii/1934, 86.

Combined premedication, drug induction, and artificial rupture of the membranes is a reliable method of inducing labour. Labour so induced lasts no longer and does not show a higher percentage of complications. Primigravidae and multigravidae with a history of defective uterine action in previous labours, receive  $1\frac{1}{2}$  gr. of quinine sulphate three times daily during the last three weeks for which the pregnancy is allowed to continue; primigravidae are admitted to

hospital 5 days before the anticipated date of artificial rupture of the membranes and multigravidae 3 days before. At 6 a.m. 1 ounce of castor oil, at 10 a.m., 2 p.m. and 6 p.m. quinine sulphate powder 10 gr., and at 5 p.m. a simple enema and a hot bath are administered to primigravidae on the day after admission (second day) and repeated on the fourth day; to multigravidae they were given on the second day.—E. C. Wise, *Brit. med. J.*, i/1939, 665.

**MALARIA.** A comprehensive test was undertaken with British troops resident in highly malarious stations in the Punjab, for the purpose of reducing the harmful effect of the autumn malarial outbreaks among the men. During the three years' duration of the test there was a uniformly lower malarial rate throughout among those taking prophylactic quinine, although it was only given for two periods of 3 weeks, with an interval of 10 days between them, in doses of 10 gr. of the sulphate daily, with the exception of Saturdays, when a purge was taken.—T. Young, *J. R.A.M.C.*, Aug., 1933; 90; *ibid.*, Apr., 1934, 269.

In the Italo-Ethiopian campaign of 1935-36, with an army of 500,000 men, there were only 1241 admissions for primary malaria and 1093 admissions for relapses, with 23 deaths from pernicious forms, including blackwater fever, and this in spite of the fact that zones of operation were badly malarial. From the beginning of the campaign quinine prophylaxis was insisted on; every soldier received three tablets a day of quinine sulphate or bihydrochloride each containing 3 gr., and care was taken to see that they took them.—A. Castellani, *Lancet*, ii/1939, 1048.

In the tropics, where malignant tertian infections are much more common, most authorities recommend a daily dosage of at least 30 gr., on account of the dangers of the development of pernicious symptoms. Although in our investigations it was found that doses of less than 30 gr. daily would have a considerable curative effect, at least as far as clinical manifestations are concerned, a daily dosage of 30 gr. is considered to be the optimum, consistent with (radical) curative action and the avoidance of harm and excessive discomfort to the patient. This dose seems to be that most usually recommended for the treatment of acute attacks in the tropics, irrespective of the kind of infection. In our work the cure rate in malignant tertian malaria, treated with quinine in doses of 20 gr., was less than half that with 30 gr. doses, given over an equal period.—J. A. Sinton, *Quart. Bull. Hlth Org. L.o.N.*, 1935, 661.

#### **Treatment of Malarial Relapses.**

The best for old cases was a system carried out by M. Harrison in an investigation of treatment under direction of Sir Ronald Ross. It was used on 49 chronic cases, mostly of benign tertian. Only 10.2% relapsed. Fever was reduced in 12 to 24 hours, and no asexual parasites could be found after 48 hours.

Patient to remain in bed 12 days (this period may be reduced) and to receive intramuscularly in each deltoid muscle 15 gr. of dihydrochloride daily with 10 gr. of quinine hydrochloride in Mixture No. 1 (*infra*) thrice daily, totalling 60 grains of quinine daily for the 12 days. Patient is then allowed up and receives for three days Mixture No. 2 four times a day (60 gr. of quinine daily by the mouth). Patient is then put on Mixture No. 3 four times daily for 14 days (20 gr. of quinine daily). Light work allowed.

[P1-81] **Anticachexia Mixture No. 1.** For a dose after food:—

Quinine hydrochloride 10 gr., tincture of ferric chloride 5 m., solution of strychnine hydrochloride 5 m., acid solution of arsenic 5 m., dilute nitrohydrochloric acid 5 m., magnesium sulphate  $\frac{1}{2}$  dr., syrup of tolu  $\frac{1}{2}$  dr., glycerin 10 m., water to 1 oz.

[P1-81] **Anticachexia Mixture No. 2.**

As No. 1, but add quinine hydrochloride 5 gr. and dilute nitrohydrochloric acid 5 m. to the dose.

[P1-81] **Anticachexia Mixture No. 3.**

As No. 1, but reduce the quinine hydrochloride 5 gr. and dilute nitrohydrochloric acid 5 m. in each dose.

For references to the use of quinine salts by injection, see the respective salts.

**Cremor Quininae (B.V.H.).** Stearic acid 2 oz. (Apoth.), sodium carbonate 131 gr., liquid paraffin 144 m., quinine 240 gr., distilled water to 20 oz. (Apoth.).

**Oleinatam Quininae (B.P.C.).** 25% w/w of quinine in oleic acid

**Quininae Acetylsalicylas (B.P.C.).**

$C_{22}H_{34}O_2N_2, C_6H_4(COOH)O \cdot OC \cdot CH_3 = 504.3.$

Dose.—1 to 5 grains (0.06 to 0.3 g.).

A white, crystalline powder containing about 64% of anhydrous quinine. M.p. 157°.

**Soluble** 1 in 330 of water, 1 in 50 of alcohol 90%, 1 in 7 of chloroform; insoluble in ether. Immediately decomposed by acids and alkalis. Antipyretic and analgesic; used similarly to quinine salicylate.

[P1-S1] **Quininæ Arsenas** (B.P.C.).  $(C_{20}H_{24}O_2N_2)_2, H_2AsO_4, 5H_2O = 934.5$ .

*Dose.*— $\frac{1}{10}$  to  $\frac{1}{2}$  grain (0.004 to 0.008 g.).

White silky needles; sparingly soluble in cold water. Contains 69% of anhydrous quinine. Owing to the small dosage of quinine possible, its action is that of arsenic. It is employed as an antiperiodic in malarial conditions.

[P1-S1] **Kinectine** (Mouneyrat, Villeneuve-la-Garenne; Anglo-French Drug Co., London). Hectine with quinine hydrochloride (i.e., benzosulpho-*p*-aminophenylarsionate of quinine). *Dose.*—3 tablets a day for 3 days and then 2 tablets every other day to a total of 18 tablets. Hay fever, coryza, influenza, malaria.

**Quininæ Benzoas** (B.P.C.).  $C_{20}H_{24}O_2N_2, C_6H_5 \cdot COOH = 446.3$ .

*Dose.*—1 to 5 grains (0.06 to 0.3 g.).

White crystals with alkaline reaction, containing 72 to 75% of anhydrous quinine. Soluble 1 in 350 of water. Has the general properties of quinine salts, but is seldom used in medicine.

**Quininæ Bisulphas** (B.P., U.S.P. XI). *Syn.* QUININÆ SULPHAS ACIDUS, NEUTRAL QUININE SULPHATE (*Fr. Cx.*, *P. Ital. V* and *F.E. VIII*).  $C_{20}H_{24}O_2N_2, H_2SO_4, 7H_2O = 548.4$ .

*Dose.*—1 to 10 grains (0.06 to 0.6 g.). U.S.P. XI average dose 15 grains. F.E. gives max. dose *per diem* 2 g.

Transparent or opaque needles containing about 59% of anhydrous quinine.

**Soluble** 1 in 10 of water and 1 in 23 of alcohol 90%.

*Uses.* Has the general properties of quinine and is preferable to quinine sulphate for the preparation of tablets, but is less suitable than the acid hydrochloride for injections, since its solution decomposes on heating. It is suitable for preparing eye lotions. In purulent ophthalmia, hypopyon and keratitis, drops containing 3 gr. with 12 gr. of boric acid per oz. are useful, and 3 gr. per oz. of water has a specific action on ophthalmic diphtheria. The 1 in 2000 solution may be used as an irrigation in cystitis.

Quinine is of value in ophthalmology on account of its astringent, bactericidal and anæsthetic properties, and because it inhibits scar-tissue formation. It may be used either in the form of a 2 to 4% quinine bisulphate ointment or in a 2% solution, and may be used with success in interstitial keratitis, trachoma, corneal opacities, vernal catarrh and phlyctenular conjunctivitis.—J. W. Robinson, *Brit. med. J. Epit.*, ii/1937, 47.

[P1-S1] **Quininæ Cacodylas**.  $C_{20}H_{24}O_2N_2, (CH_3)_2AsO \cdot OH = 462.2$ .

*Dose.*—*Per os* and hypodermically  $\frac{1}{2}$  to 1 grain (0.016 to 0.06 g.). Larger doses are sometimes given.

White acicular crystals soluble in water. This salt has been suggested for intravenous use in malaria,  $7\frac{1}{2}$  grains (0.5 g.) in 20 ml. It has approximately the same toxicity as quinine dihydrochloride and dihydrobromide.

**Quininæ Camphoras**.  $(C_{20}H_{24}O_2N_2)_2, C_6H_4(COOH)_2 = 848.5$ .

*Dose.*—1 to 10 grains. An insoluble powder.

**Transpulmin** (Camden Chemical Co., London). Solution of basic quinine and camphor in volatile oils. *Dose.*—1 to 2 ml. intramuscularly per day for from 7 to 21 days. Influenza, bronchitis, broncho-pneumonia, etc.

**Quininæ Citras** (B.P.C.).

$(C_{20}H_{24}O_2N_2)_2, C_6H_4 \cdot OH(COOH)_2, 7\frac{1}{2}H_2O = 1300$ .

*Dose.*—1 to 5 grains (0.06 to 0.3 g.).

Soluble 1 in 900. It has, therefore, little taste. Given suspended in mixture. Contains about 74.5% of anhydrous quinine.

**Ferri et Quininæ Citras (B.P., P. Dan.).**

*Dose.*—5 to 15 grains (0.3 to 1 g.). 15 gr. contains about 2 gr. of iron and  $2\frac{1}{2}$  gr. of quinine.

It may be given in solution, or in pills with simple syrup or mucilage of acacia (not in excess, as, unless made very hard, they lose shape). Alcohol 60% with glycerin 5% is also a suitable excipient. Greenish-yellow deliquescent scales with bitter chalybeate taste. Contains about 13% of Fe and 15% (P. Dan. 10%) of anhydrous quinine. Largely used as a general tonic.

*Soluble* 2 in 1 of water.

*Incompatible* with tannin and alkalis, also with phosphoric acid (ferric phosphate may be thrown out) unless considerably diluted prior to mixing.

**Vinum Ferri et Quininæ (B.P.C.).** *Dose.*—1 to 4 drachms (4 to 16 ml.). Contains 1 grain of iron and quinine citrate per drachm of sherry-type wine. [P.] **Sirop Neurotonique.**

*Dose.*—2 to 3 drachms (8 to 12 ml.) in a little water after meals. Iron and quinine citrate 0.50, strychnine nitrate 0.01, liquid extract of kola 5.0, sodium glycerophosphate 5.0. Dissolve with slight heat in syrup of orange, q.s. to 100.

**Quininæ Dihydrobromidum (B.P.C.).** *Syn.* QUININÆ HYDROBROMIDUM ACIDUM. (Fr. Cx. "Neutral").

$C_{20}H_{24}O_2N_2 \cdot 2HBr \cdot 3H_2O = 540.1$ .

*Dose.*—1 to 10 grains (0.06 to 0.6 g.). Hypodermically, 3 to 5 grains (0.2 to 0.3 g.).

In yellowish rectangular prismatic crystals, or in powder. Contains about 60% of anhydrous quinine.

*Soluble* 1 in 7 of water; very soluble in alcohol, but insoluble in ether. It is well adapted for hypodermic injection. It is non-irritating. The additional hydrobromic radical tends to prevent quinism.

**Quininæ Dihydrochloridum (B.P., U.S.P. XI, P. Helv. V).** *Syn.* QUININÆ HYDROCHLORIDUM ACIDUM, QUININE DI- OR TRI-HYDROCHLORIDE.  $C_{20}H_{24}O_2N_2 \cdot 2HCl = 397.1$ . *Fr. Cx., P. Ital. V and F.E. VIII* term this "neutral" quinine hydrochloride.

Crystallised from alcohol, the salt contains alcohol and water of crystallisation. Left exposed to the air, this loses its alcohol and the salt changes to one with  $2\frac{1}{2}$  molecules of water, becoming at the same time opaque. This was formerly official in *Fr. Cx.*

*Dose.*—1 to 10 grains (0.06 to 0.6 g.). By intravenous and intramuscular injection, 5 to 10 grains (0.3 to 0.6 g.). *U.S.P. XI* average dose 15 grains. *F.E. VIII* has max. daily dose 2 g.

A white powder containing 81.6% of quinine.

*Soluble* 1 in 0.6 of water, 1 in 12 of alcohol 90%.

It should not be administered parenterally in a concentration exceeding 1 gr. per ml. To prepare sterile solutions colourless quinine acid hydrochloride is dissolved in freshly distilled water and the solution filtered through a Berkefeld filter. It is filled into ampoules and sterilised by boiling once in a water-bath for half an hour. Such a solution should keep for a considerable time, because the drug tends to be self-sterilising.—O. Turner, *Trans. R. Soc. trop. Med. Hyg.*, 1940, 34, 111.

*Uses.* This is the most suitable salt for the preparation of solutions for injection. Although quinine is best administered by

mouth in the great majority of cases, intramuscular or intravenous injections are a valuable procedure in acute cases of pernicious malaria, especially when accompanied by constant vomiting or symptoms suggestive of cerebral involvement. Subcutaneous injections are seldom employed, since they are liable to be followed by fibrous induration.

**INTRAMUSCULAR INJECTIONS.** It is preferable to use a dilute solution, *e.g.*, 0.5 to 0.6 g. in 3 or 4 ml. of normal saline, sterilised by boiling and cooled before injection. The best site for injection is in the gluteus muscle,  $1\frac{1}{2}$  to 2 inches below the crest of the ileum, avoiding the line of the sciatic nerve, since infiltration of the tissues in the neighbourhood of the large nerve trunk may cause serious and permanent damage. The injection should be given with the strictest asepsis, since the drug causes a localised necrosis, and lack of aseptic precautions may cause infection of the necrotic area resulting in abscess formation and possibly even tetanus. The injections should not be given in the same place every day, and they should be stopped and quinine given by the oral route as soon as the paroxysms have been controlled.

**INTRAVENOUS INJECTIONS.** These may be given when rapid action is required, as in cerebral malaria. The dose is usually 0.6 g. dissolved in 10 ml. of normal saline. The injection should be given slowly (at least ten minutes being allowed) with the patient in a recumbent position, and with the strictest aseptic precautions. Alternatively, the injection may be made with a gravity apparatus, using 0.6 g. dissolved in 100 ml. of normal saline. A single intravenous injection, repeated if necessary on the following day, generally clears the condition sufficiently to allow of the resumption of oral administration. Care must be taken to ensure that the injection does not infiltrate the walls of the vein or the subcutaneous tissue, or sloughing and fibrosis may result. The injection causes a rapid fall of blood pressure and affects the respiratory centre, and a careful watch must therefore be kept on the patient's heart, pulse and respiration. It should be employed with special precaution in the presence of organic disease of the heart, albuminuria, severe jaundice, marked anæmia, or debility, and idiosyncrasy to quinine.

In addition to their use in malaria, intravenous injections of quinine were at one time advocated in the treatment of pneumonia and puerperal septicæmia, but their use in these conditions has now been largely abandoned. Excellent results are said to have been obtained in the treatment of paroxysmal tachycardia by intravenous injections, in doses up to  $7\frac{1}{2}$  grains, the attack ceasing abruptly while the injection is being given.

Intramuscular injections condemned in ordinary cases of malaria, but intravenous injections (quinine dihydrochloride 0.6 g. in 5 ml. physiological saline) recommended in serious cases of malignant tertian associated with persistent vomiting or threatened coma.—S. P. James, *Brit. med. J.*, ii/1933, 929.

Oral method the only method of administering cinchona alkaloids, though rarely in grave cases, *e.g.*, cerebral malaria, quinine base should be injected



intravenously.—H. W. Acton and R. N. Chopra, *Indian J. med. Res.*, Oct., 1924, 251; see also J. Macqueen, *Lancet*, i/1927, 1289.

Intramuscular injections given in large numbers without tetanus being caused (as result of muscle fibre necrosis). Pain does not occur unless some solution gets into the subcutaneous tissues. However, intravenous injections are more rapid and painless. 0.6 g. in 10 ml. water.—M. S. Nawaz Ahmadi, *Brit. med. J.*, ii/1930, 621.

**Lotio Quininae Hydrochloridi (R.L.O.H.).** Quinine dihydrochloride 4 gr., sterilised water to 1 oz. For corneal ulcers.

[D-P1-81] "**Old English**" Fever Powder. Quinine dihydrochloride 3 gr., arsenious acid  $\frac{1}{10}$  gr., compound soap pill 1 gr., calomel  $\frac{1}{10}$  gr. 3 times daily in a cachet. Malaria well treated. The following [D-P1-81] daily dose made up in the form of a pill recommended as prophylactic:—Quinine dihydrochloride  $1\frac{1}{2}$  gr., arsenious acid  $\frac{1}{10}$  gr., compound soap pill  $\frac{1}{10}$  gr., calomel  $\frac{1}{10}$  gr.

**Quininae Disalicyclosalicylas (B.P.C.).** *Syn. and Prop. Name.* QUININAE BISALICYCLOSALICYLAS, QUINISAN (*Howards, Ilford*).  
 $C_{26}H_{24}O_2N_2 \cdot 2C_6H_4(COOH) \cdot O \cdot CO \cdot C_6H_4(OH) = 840.4$ .

*Dose.*—1 to 5 grains (0.06 to 0.3 g.).

White microcrystalline powder with slightly bitter taste. Contains about 39% of anhydrous quinine. For influenza, coryza, tonsillitis, neuralgia, etc.

**Quininae et Aethylis Carbonas (B.P., U.S.P. XI, Fr. Cx., etc.).** *Prop. Name.* EUQUININE (*Bayer Products, London*).  
 $C_{20}H_{23}O_2N_2 \cdot CO_2 \cdot C_2H_5 = 396.2$ .

*Dose.*— $1\frac{1}{2}$  to 15 grains (0.1 to 1 g.) in cachet. *F.E. VIII* gives max. *per diem* 1 drachm approx.

White needle crystals, m.p.  $90^\circ$  to  $92^\circ$  (*B.P. Add. I* not below  $90^\circ$ ), with little taste.

**Soluble** sparingly in water, more so by addition of dilute acid; soluble 1 in 2 of alcohol 90%, 1 in 10 of ether, 1 in 1 of chloroform.

Useful as an almost tasteless form of quinine, especially for children. Whooping cough has been treated with it; it is sometimes useful in lessening the severity and frequency of the spasms.

**Chininum Carbonicum (Fr. Cx., P. Ital. V, P. Ned. V).** *Syn. and Prop. Name.* QUININE CARBONATE, ARISTOQUININE, ARISTOCHIN (*Bayer Products, London*).  
 $CO(C_{20}H_{23}O_2N_2)_2 = 674.4$ .

*Dose.*—1 to 10 grains (0.06 to 0.6 g.) according to age.

A white tasteless powder. Obtained by heating quinine with phenyl carbonate. Insoluble in water. Used in malaria, typhoid, influenza and pertussis as a tasteless substitute for quinine. Incompatible with acids and alkalis.

**Quininae et Ureae Hydrochloridum (B.P.C., U.S.P. XI).**  
*Syn.* QUININAE HYDROCHLORO-CARBAMIDUM, UREA-QUININE.  
 $C_{20}H_{24}O_2N_2 \cdot HCl, CO(NH_2)_2, HCl, 5H_2O = 547.3$ .

*Dose.*— $\frac{1}{2}$  to 15 grains (0.03 to 1 g.), by injection. *U.S.P. XI* average hypodermic dose (once daily) 15 grains.

In small prisms, soluble 1 in about 1 of water. Contains about 59% of anhydrous quinine.

**Uses.** Mainly used as a local anæsthetic in doses of 3 to 5 ml. of 0.5 to 1% solution, especially for rectal operations where post-operative pain is severe, since its anæsthetic effect may last for several hours or even days. For internal hæmorrhoids the 5% solution is used, using a few minims for each pile, or the whole area may be treated by submucous injection. The method should

not be employed for external, sloughing or strangulated hæmorrhoids, or where there is local infection of the ano-rectal region. Suppositories (5 gr.) and ointment (20%) are also of value in hæmorrhoids and other painful conditions of the rectum. The injection of 4 m. of the 5% solution, repeated if necessary at 2 to 3-day intervals, has been used in anal fissure. For local application strong solutions (10 to 20%) must be used to ensure passage through the mucous membrane, and have been found of value in tonsillitis and painful throat affections.

Deep intramuscular injection of 5 ml. of 1% solution is useful in lumbago, sciatica and neuritis.

**EXOPHTHALMIC GOITRE** and thyroid enlargement treated by injections of 4 to 8 ml. of a 4% solution of quinine and urea hydrochloride into the thyroid. After a few treatments the goitre becomes smaller and when it is one-third of original size the treatment can be stopped, as the shrinking will continue until no tumour is perceptible. The drug is believed to act through its necrotic action on the parenchyma of the gland.—H. G. Loughran, per *Prescriber*, 1927, 173.

**HÆMORRHOIDS.** The injection is to be given between the vein and the mucous membrane of the rectum, and not in the vein itself. It is seldom necessary to give more than 3 ml. at one sitting. Injections given at weekly intervals, 6 to 8 being the average number required.—C. Howard, *Lancet*, i/1929, 20.

Sloughing after 5% injection in hæmorrhoids. Never inject an external pile or a prolapsed pile without first reducing it and never inject a pile that is already sclerosed.—*Lancet*, i/1930, 1027.

**HYDROCELE.** The injection treatment of hydrocele is favourably reported upon on all sides, the best sclerosing agent being quinine and urea hydrochloride, 3 to 5 ml. The hydrocele is tapped; after washing out the sac with more saline the solution is introduced into the hydrocele sac. The scrotum is then massaged. Although the fluid in the sac reaccumulates, within 3 or 4 weeks the exudate is generally absorbed.—H. Bailey, *Med. Annu.*, 1935, 429.

**WOUNDS.** For wounds which are to heal by granulation, quinine urea hydrochloride 1 in 600 should be liberally injected as a prophylactic against pain.—R. E. Farr, *Lancet*, ii/1929, 1199.

**Quininae Formas** ("Basic" in France). *Syn. and Prop. Name.* QUINIFORM, CHINIFORM (*Chinosolfabrik, Hamburg; C. Zimmermann, London*).

$C_{20}H_{34}O_2N_2 \cdot H \cdot COOH \cdot H_2O = 388.2$ .

*Dose.*—1 to 5 grains (0.06 to 0.3 g.). Subcutaneously, 1 to 3 grains. (Stated not to be painful.)

White crystals, m.p. about 126°.

**Quininae Formas Acidus** ("Neutral" in France).

$C_{20}H_{34}O_2N_2 \cdot (H \cdot COOH)_2 = 416.2$ .

*Dose.*—1 to 5 grains (0.06 to 0.3 g.).

Long white needles; m.p. 95°.

**Quininae Hydriodidum** (B.P.C.). *Syn.* QUININE IODIDE.

$C_{20}H_{34}O_2N_2 \cdot HI = 452.1$ .

*Dose.*—1 to 5 grains (0.06 to 0.3 g.).

Pale yellow crystals slightly soluble in cold water, readily in hot water and in alcohol. Contains about 72% of anhydrous quinine. Has been used in chronic rheumatism.

**Quininae Dihydriodidum.** *Syn.* QUININÆ HYDRIODIDUM ACIDUM.

$C_{20}H_{34}O_2N_2 \cdot 2HI \cdot 5H_2O = 670.2$ .

*Dose.*—1 to 5 grains (0.06 to 0.3 g.).

Pale yellow crystals or scales, soluble 1 in 20 of water.

**Quininae et Urethani Hydrochloridum.**

*Dose.*— $\frac{1}{2}$  to 3 grains (0.03 to 0.2 g.).

Employed hypodermically, as it is non-irritating.

Obtained by heating quinine hydrochloride 3 with urethane 15 and water 3 parts.

**Uses.** This is employed mainly by injection as a sclerosing agent in varicose veins, varicocele, hæmorrhoids and nævi. It is said to be less painful than sodium salicylate and safer than sodium morrhuate.

### **Injectio Quininae et Urethani (B.P.C.).**

**Dose.**—75 minims (5 ml.), by intravenous injection.

Quinine hydrochloride 13.33% *w/v* and urethane 6.67% *w/v* in water. *Fr. Cx.* has 40% and 20% respectively.

ANGIOMA OF THE LOWER LIP treated by 14 injections over 6 months, commencing with 0.5 and increasing to 1 ml. Injections through sound skin near margin of tumour. Treatment painless.—Graham, *J. R.A.M.C.*, April, 1930.

HÆMORRHOIDS treated with quinine hydrochloride 0.8 g., urethane 0.4 g. in normal saline 2 ml.—Bellot, *Lancet*, i/1929, 1072.

Good results by injection of 3 to 5 ml. of 5% solution perivenously (into the submucous tissue round the piles), repeating the injection at weekly intervals on opposite sides.—A. H. Douthwaite, *The Injection Treatment of Varicose Veins* (H. K. Lewis), 5th Edn., 1929.

HYDROCELE OF THE TUNICA VAGINALIS treated by injection of quinine-urethane solution 2 ml. without pain or discomfort.—F. C. Pybus, *Brit. med. J.*, i/1930, 239.

NÆVI cured by injection of a minim of quinine and urethane solution into 4 or 5 different places in the nævus, repeated two or three times at fortnightly intervals.—G. B. Dowling, *Lancet*, ii/1929, 1251; *Med. Annu.*, 1931, 324.

Cavernous nævi involving the left breast and the buttock, in a girl aged 9 months, successfully treated by this method. Excision should be relegated to the past.—A. P. Bertwistle, *Lancet*, i/1934, 22.

A 20% solution of quinine dihydrochloride and urethane diluted with an equal part of 2% procaine hydrochloride (with adrenaline), was found a painless and effective sclerosing solution for vascular birthmarks in infants. From 0.1 to 0.2 ml. is injected at a time, the needle being so directed that the solution is initially injected superficially throughout the mass. Immediate blanching of the area occurs about the needle point, the needle is then advanced and the next injection placed so that its area of blanching is contiguous with the previous one. Multiple areas are thus injected until the entire lesion has been mottled with areas of blanching. 44 hemangiomas were thus treated in 30 infants varying from 2 weeks to 3 years, all with excellent ultimate results and without systemic reactions.—H. W. Kæssler, *J. Amer. med. Ass.*, i/1938, 1644.

VARICOCELE successfully treated by quinine-urethane injection (Douthwaite's formula)—one injection of 1 ml.—H. M. Hanschell, *Brit. med. J.*, ii/1928, 915.

### **Quinine and Urethane Injection Treatment of Varicose Veins.**

The injection contains quinine hydrochloride 4 g., urethane 2 g. in distilled water 30 ml. (Injectio Quininae et Urethani B.P.C.). The solution can be boiled and is strongly antiseptic. It crystallises out when cool but redissolves on immersing in hot water for a few seconds. The syringe should be warmed before filling with the solution.

**Contraindications:** Deep thrombosis, acute phlebitis, intra-abdominal tumours, cardiovascular disease, skin diseases, pregnancy. The injection should not be given during menstruation.

**Initial Injection**  $\frac{1}{2}$  ml., and subsequently 2 to 3 ml. Injections may be given with the patient sitting or lying down—in the latter case, a pneumatic tourniquet is applied to the middle of the thigh

before the patient lies down. Clean the skin with ether and introduce needle of syringe not quite filled with solution into the lowest segment of the vein, the skin overlying the vein being drawn aside before introducing the needle. Withdraw the piston slightly and allow blood to flow into the barrel before any fluid is introduced. Inject  $\frac{1}{4}$  to  $\frac{1}{2}$  ml. according to size of vein and hold needle in position for 30 seconds before withdrawal. Press a pledget of wool on puncture and repeat the process 4 inches up the limb. When the total number of injections has been given, clean with ether and seal punctures with collodion dressings. Sitzings are given at weekly intervals, 6 sittings usually sufficing. Injections may be successfully given, without fear, in the region of the saphenous opening.

Injections of 2 ml. can generally be relied on to thrombose 5 to 6 inches of a vein. Injections are needed at approximately 4 to 5 inches along the course of a vein. In this way the whole saphenous tract may be treated to within about 4 inches of the saphenous opening.

**After-effects.** Patients should be told that small and thin-walled veins will swell up rapidly to four times their original size. The swelling passes off in a few hours and is of no importance. Sensations of fullness, aching or tenderness sometimes occur lasting three or four days; a feeling of contraction of the leg, one month after obliteration of the internal saphenous vein, passes off in a few weeks. Œdema of foot and leg occurs in about 2% of cases from 5 to 7 days after injection, persisting for some two weeks. Itching of the overlying skin (following treatment by any sclerosing solution) is relieved by application of ichthammol and Lassar's paste.

Quinine-urethane solutions appear to be the most certain in their thrombosing action; with the empty-vein technique and small doses they are extremely efficient. Quinine-urethane solutions have the additional advantage of being painless during injection.—R. T. Payne, *Brit. med. J.*, i/1936, 878.

The solution is not painless and can excite allergy, and personal idiosyncrasy is a danger. In busy clinics the patients seem to faint rather frequently and the women patients often have very violent uterine colic on the way home and premature menstruation next day.—A. Dickson Wright, *Brit. med. J.*, i/1940, 665.

**Giemsa's Injection** contains quinine hydrochloride 10 g., urethane 5 g., water 18 ml. The volume of the product is 30 ml., so that 1.5 ml. of solution contains 0.5 g.

**Solutio Quininae et Urethani** (for varicose veins) (*St. T.H.*).

**Dose.**—5 ml. intravenously.

Quinine hydrochloride 5% and urethane 2½% in distilled water.

**Chinethan** (*Richter, London*). A quinine and urethane preparation for injection. **Dose.**—2 ml. daily for three days intramuscularly, or 1 ml. once or twice weekly intravenously. Intramuscularly for malaria, pneumonia, influenza, etc., intravenously for varicose veins.

**Varixol** (*Evans, Sons, Lescher & Webb, Liverpool*). Quinine and urethane solution for the injection treatment of varicose veins.

**Quininae Hydrobromidum** (*B.P.C.*). (*P. Belg. IV, Fr. Cx. and P. Ital. V* term this "basic" quinine hydrobromide, and have 1 H<sub>2</sub>O.)

**Syn. QUININE BROMIDE.**  $C_{20}H_{24}O_2N_2.HBr.2H_2O = 441.2$ .

**Dose.**—1 to 10 grains (0.06 to 0.6 g.) or more.

White acicular crystals, soluble 1 in 55 of water, 1 in 0.7 of alcohol 90%. Contains not less than 73% of anhydrous quinine.

**Uses.** Quinine is given with an excess of hydrobromic acid to lessen the cinchonism sometimes caused by large doses. The sedative action is useful in neuralgia and acute rheumatism. In exophthalmic goitre  $2\frac{1}{2}$  gr. doses thrice daily are said to have given good results. Tropical abscess has been treated by aspiration and injecting into the cavity a 1% solution.

**Quininae Hydrochloridum** (B.P., P. Helv. V, etc.). F.E. VIII, P. Belg. IV and Fr. Cx. term this "basic" quinine hydrochloride. Syn. QUININE HYDROCHLORATE.

$C_{20}H_{24}O_2N_2 \cdot HCl \cdot 2H_2O = 396.7$ .

**Dose.**—1 to 10 grains (0.06 to 0.6 g.). F.E. has max. daily dose 2 g.

Contains about 82% of anhydrous quinine. Efflorescent in warm air.

**Soluble** 1 in 32 of water, 1 in 2 of 90% alcohol, about 1 in 1 of chloroform, but insoluble in acetone. Quinine hydrochloride 2 with phenazone 1 will dissolve in 4 of water.

**Insoluble.** Similar to quinine sulphate.

**Uses.** Quinine hydrochloride is more soluble and more readily absorbed than quinine sulphate, and is less irritating to the gastric mucosa. It is employed similarly to the sulphate in malaria and may also be used by injection, though for this purpose the dihydrochloride is more usually employed.

For the paroxysmal headache or neuralgia so common after malaria the following mixture is recommended:—Quinine hydrochloride 3 gr., tincture of cimicifuga 5 m., caffeine citrate 2 gr., spirit of chloroform 10 m., compound infusion of orange to 1 oz., twice daily.

In acute tonsillitis, quinine hydrochloride internally and as mouth-wash is useful; also with dilute nitric acid in cachectic cases of vesicular stomatitis. In conjunction with urethane, quinine hydrochloride is extensively used in the injection treatment of varicose veins, see p. 881.

**LOCAL ANÆSTHESIA IN TONSILLECTOMY.** Quinine hydrochloride  $\frac{1}{2}$  gr. in 2 dr. of water is said to be superior to 0.2% cocaine (5 ml.). A small amount of 20% cocaine is first applied.

**MYOTONIA.** From  $2\frac{1}{2}$  to 5, 10, or 15 gr. of quinine hydrochloride two or three times a day by mouth consistently eliminates myotonus as a disturbing symptom.—F. Kennedy and A. Wolf, *J. Amer. med. Ass.*, i/1938, 198.

**Collyrium Quininae Hydrochloridi** (B.P.C.). 0.5% w/v.

[P1] **Mistura Quininae et Magnesii Sulphatis** (L.H.). Quinine hydrochloride 1 gr., magnesium sulphate 30 gr., dilute hydrochloric acid 1 m., solution of arsenic 3 m., solution of strychnine hydrochloride 3 m., water to 1 oz. For use during treatment of stomatitis and gingivitis.

**Nebula Quininae.** Quinine hydrochloride 10 gr., glycerin and rose water to 1 oz.

**Pessus Quininae Hydrochloridi** contains 3 gr. (0.2 g.) in 30 gr. of oil of theobroma. A valuable remedy for leucorrhœa. Also used as a contraceptive. #

Contraceptive action of pessaries with cocoa butter basis probably largely due to mechanical action, *i.e.*, the covering of the cervix with a thin film impeding the ingress of the spermatozoa.—*Lancet*, ii/1931, 258.

At the B.M.A. Cent. Meeting, 1932 (Sect. of Dermat. and Vener. Dis.) several speakers quoted cases of dermatitis, due to quinine idiosyncrasy, following the use of quinine pessaries.—*Lancet*, ii/1932, 399.

Now that substances are available which are not only more spermicidal but also free from any harmful and remote effects on the users, it would seem that the time has come to abandon the use of quinine for contraceptive purposes.—*Lancet*, ii/1935, 1133.

**Rendell's Quinine Pessaries** (*W. J. Rendell, London*). Pessaries weigh 36.6 gr. and contain 3.5% of quinine, equivalent to 2.16 gr. of quinine acid sulphate.

For further references to contraceptives, see under *Acidum Lacticum*, *Chloramina*, *Potassii Hydroxyquinolini Sulphas* and *Hexyl-resorcinol*.

[D-P1-81] **Pulvis Quininae, Arseni, Hydrargyri et Ipecacuanhae Compositus**.

Quinine hydrochloride 5 to 7 gr., arsenious acid  $\frac{1}{16}$  to  $\frac{1}{8}$  gr., Dover's powder 3 to 4 gr., calomel  $\frac{1}{16}$  to  $\frac{1}{8}$  gr. In a cachet; one to be taken at 11 a.m. and another at bedtime. In chronic malaria with enlarged spleen.

**Solutum Chinini Compositum** (*Fr. Cx.*).

Quinine hydrochloride 3 g., phenazone 2 g., boiled and cooled distilled water to 10 ml. Special instructions as to sterilisation are provided.

**Tinctura Quininae** (*B.P.C.*). *Dose*.— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Quinine hydrochloride 1, tincture of orange 50. A very agreeable form of taking small doses of quinine.

**Vinum Quininae** (*B.P.C.*). *Dose*.— $\frac{1}{2}$  to 1 ounce (16 to 30 ml.).

Contains 1 gr. of quinine hydrochloride dissolved in 1 oz. of orange wine.

*The Customs and Excise Commissioners allow the sale of quinine wine without licence if:—(a) It is prepared in accordance with the B.P.C.; (b) Sales are made only by duly qualified chemists and druggists; and (c) It is labelled to show that it is to be used as a medicine. The word "Dose" should appear on the label in bold type. This should not exceed the B.P.C. dose, but the Board do not object to the use instead of the words "one or two tablespoonfuls," or "half a wineglassful."*

**Solvochin** (*Camden Chemical Co., London*). Water-soluble quinine ("quinine-hydrate-phenazone-basic quinine-hydrochloride"). *Dose*.—In pneumonia, 2 ml. daily on 3 successive days, intramuscularly; in malaria and obstetrics (to promote uterine contraction), 1 or 2 intramuscular injections of 2 ml. daily.

**Solvochin-Calcium** (*Camden Chemical Co., London*). A preparation of Solvochin with calcium glutamate, one 5 ml. ampoule containing 250 mg. of quinine as hydrochloride and 72 mg. of calcium. In pneumococcal pneumonia. *Dose*.—One ampoule (5 ml.) once or twice daily by intragastral injection.

**Quinine Hypophosphis** (*B.P.C.*).  $C_{20}H_{24}O_2N_2 \cdot H_2PO_2 \cdot 2H_2O = 426.3$ .

A white crystalline or amorphous powder, soluble 1 in 24 of water and 1 in 40 of alcohol 90%. Contains about 75% of anhydrous quinine.

**Quinine Lactas** (*B.P.C.*).  $C_{20}H_{24}O_2N_2 \cdot CH_2 \cdot CHOH \cdot COOH = 414.3$ .

*Dose*.—1 to 5 grains (0.06 to 0.3 g.).

A crystalline or granular white powder, soluble 1 in 6 of water. Said to be well tolerated; is suitable for hypodermic injection. Contains not less than 72% of anhydrous quinine.

A 1% solution has been used as an injection in gonorrhoea.

**VARICOSE VEINS**. Preferable to the hydrochloride which is apt to cause severe reactions. Employed as a 10 or 15% solution, also as a saturated solution

(16.6%) on 170 patients, with good results. It is self-sterilising in solutions above 1% and solutions keep well. The dose for each injection varies from 0.25 to as much as 3 ml. in large veins.—J. W. Riddoch, *Lancet*, ii/1934, 1101.

**Quininae Phosphas** (B.P.C.). ( $C_{20}H_{14}O_2N_4$ )<sub>2</sub>·2H<sub>3</sub>PO<sub>4</sub>·6H<sub>2</sub>O = 1277.0.

Dose.—1 to 5 grains (0.06 to 0.3 g.).

In acicular crystals like the sulphate, but harder and denser. Contains about 75% of anhydrous quinine. Soluble 1 in 850 of water and 1 in 110 of alcohol 90%.

**Quininae Salicylas** (B.P.C., F.E. VIII, P. Ital. V).

$C_{20}H_{24}O_2N_4$ ·C<sub>6</sub>H<sub>4</sub>(OH)·COOH·H<sub>2</sub>O = 480.3.

Dose.—1 to 5 grains (0.06 to 0.3 g.).

White crystals, sparingly soluble in water, and about 1 in 24 of alcohol 90%. Incompatible with mineral acids—salicylic acid may crystallise out. Contains about 69% of anhydrous quinine. Should be given in cachets, or pills made with syrup of glucose, or as quinine salicylate mixture. Given to abort the common cold, in influenza and in neuralgia, rheumatism and sciatica.

**Mistura Quininae Salicylatis** (B.P.C.).

Dose.— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.).

Contains ammoniated solution of quinine 30 m., sodium salicylate 10 gr., and potassium citrate 10 gr. in glycerin and compound infusion of gentian to 1 oz.

**Quininae Sulphas** (B.P.). (Termed "BASIC" QUININE SULPHATE in *Fr. Cx.*, *P. Ital. V.* and *F.E. VIII*).

( $C_{20}H_{24}O_2N_4$ )<sub>2</sub>·H<sub>2</sub>SO<sub>4</sub>·7 $\frac{1}{2}$ H<sub>2</sub>O = 881.6. Water content varies among the National Pharmacopœias. *P. Jap.*, F.E. VIII, P. Ital. V, *P. Ned. V* and *P.G. VI*, 8H<sub>2</sub>O; *P. Belg.*, 7H<sub>2</sub>O; *U.S.P. XI*, *Fr. Cx.* and *P. Helv. V*, 2H<sub>2</sub>O; *P. Dan.*, 7 to 8 H<sub>2</sub>O.

Dose.—1 to 10 grains (0.06 to 0.6 g.). *U.S.P. XI* average dose 15 grains. *F.E. VIII* gives max. daily dose 2 g.

White silky crystals containing about 75% of anhydrous quinine.

**Soluble** 1 in 800 of cold water, 1 in about 65 of alcohol 90%, 1 in 40 of glycerin.

It is prescribed in pill, cachet, tablet or mixture—if in mixture 1 m. of dilute sulphuric acid per gr. of sulphate will render soluble (with fluorescence).

**Incompatible** with alkalis and alkaline carbonates, also incompatible with Liquor Ammonii Acetatis (unless distinctly acid in reaction), iodides and astringent infusions containing tannin.

**Uses:** Quinine sulphate has the general properties of quinine and is the most commonly used of the salts. Large doses are given in malaria and intermittent fevers and smaller doses in continued fevers and neuralgia, and to improve the appetite. A mixture frequently employed in hospitals is 5 to 10 gr. of quinine sulphate with 5 to 10 m. of dilute sulphuric acid in an ounce of water; this is more rapidly absorbed than powder or tablets. For external use 0.5% solutions may be employed as a spray in hay fever and a 0.2% solution is of value in corneal ulcer.

**MYOTONIA.** By giving 0.6 g. of quinine sulphate by mouth three or four times daily patients with myotonia atrophica can be kept free from the symptoms of myotonia. Smaller doses are ineffective and the treatment must be continued almost indefinitely.—Kolb, Harvey and Whitehill, per *Brit. med. J.*, ii/1938, 77.

**Capsulæ Quininae Ammoniatæ (B.P.C.).** *Dose.*—1 capsule. Contain quinine sulphate and ammonium bicarbonate approximately equivalent to 1 dr. of ammoniated solution of quinine.

**Capsulæ Quininae Ammoniatæ et Cinnamomi (B.P.C.).**

*Dose.*—1 capsule.

Similar to the preceding but containing also  $\frac{1}{2}$  m. of oil of cinnamon.

**Capsulæ Quininae et Cinnamomi (B.P.C.).** *Dose.*—1 capsule.

Quinine sulphate 1 gr., oil of cinnamon 1 m.

**Collunarium Quininae.** Quinine sulphate 1, water 1000.

Used in hay-fever. If a stronger solution be required, use the acid sulphate or hydrochloride of quinine; avoid excess of acid.

**Elixir Quininae Ammoniatum et Cinnamomi (B.P.C.).**

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

A flavoured preparation of approximately the same strength as ammoniated solution of quinine and containing also oil of cinnamon. When using this formula the volume of syrup of orange should be reduced to 7 fluid ounces.

**Liquor Quininae Ammoniatæ (B.P.).** *Syn.* TINCTURA QUININÆ AMMONIATA. *Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Quinine sulphate 2% and dilute solution of ammonia 10%, in alcohol (60%). The quinine precipitates on adding to water; mucilage of tragacanth will suspend the precipitate. With syrup of orange it is palatable, and bears dilution better; it remains bright if mixed with aerated water. Should be kept in the dark, or it will become discoloured.

Ammoniated Quinine Tablets are prepared, each equivalent in quinine sulphate to 1 drachm of the preceding solution, but the ammonia content is variable.

**Mistura Chlori cum Quinina (Burney Yeo).**

To potassium chlorate, in powder, 30 gr., in a 12-ounce bottle, add hydrochloric acid 60 m.; cork and shake well to liberate chlorine; absorb this by gradually adding, and shaking after each addition, distilled water *q.s.* to 11 oz.; add quinine sulphate 24 gr. (or 36 gr. if ordered), syrup of orange 1 oz. *Dose.*—1 ounce (30 ml.) every 2, 3, or 4 hours for typhoid; it quickly cleanses the tongue.

**Mist. Ferri et Quin. (N.I.F.).** Quinine sulphate 1 gr., solution of ferric chloride 10 m., dilute hydrochloric acid 1 m., chloroform water to  $\frac{1}{2}$  oz.

**Mistura Quininae Ammoniatæ (St. M. H.).**

*Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.).

Ammoniated solution of quinine 1 dr., dilute solution of ammonium acetate 2 dr., sodium nitrite 1 gr., mucilage of tragacanth 1 dr., chloroform water to 1 oz.

[P1] **Mistura Quininae Composita (L.H.).** *Syn.* BROADBENT'S MIXTURE.

Ammoniated solution of quinine 1 dr., strong solution of ammonium acetate 15 m., camphorated tincture of opium  $\frac{1}{2}$  dr., ammonium carbonate 2 gr., tragacanth  $\frac{1}{2}$  gr., peppermint water to  $\frac{1}{2}$  oz.

**Mistura Quininae Effervescens.**

Quinine has a reputation in colds, but it is best given in effervescent mixtures. The following prescription is useful:—

**Mixture A.**—Quinine sulphate 2 $\frac{1}{2}$  gr., citric acid 10 gr., water to  $\frac{1}{2}$  oz.

**Mixture B.**—Potassium bicarbonate 10 gr., ammonium carbonate 2 $\frac{1}{2}$  gr., syrup of orange 1 dr., water to 1 oz.

One tablespoonful of mixture (A) with two of mixture (B) in effervescence thrice daily.

[P1] **Mist. Quin. et Gelsem. (N.I.F.).** Quinine sulphate 1 $\frac{1}{2}$  gr., potassium bromide 7 $\frac{1}{2}$  gr., dilute hydrobromic acid 7 $\frac{1}{2}$  m., tincture of gelsemium 7 $\frac{1}{2}$  m., chloroform water to  $\frac{1}{2}$  oz.

**Mist. Quin. Sulph. (N.I.F.).** Quinine sulphate 1 $\frac{1}{2}$  gr., dilute hydrobromic acid 10 m., concentrated infusion of orange 7 $\frac{1}{2}$  m., chloroform water to  $\frac{1}{2}$  oz.



**[D-P1-81] Pilula Quininae, Hydrargyri et Opii.**

Quinine sulphate  $1\frac{1}{2}$  gr., grey powder 1 gr., opium  $\frac{1}{2}$  gr., quassia extract *q.s.*, thrice daily after food. In syphilis quinine is useful before or after a course of mercury.

**Pilulae Quininae Sulphatis (B.P.C.).** *Dose.*—1 to 4 pills. 2 gr.

**[P1] Rhinitis Tablets (Parke, Davis, London).** Powdered camphor  $\frac{1}{2}$  gr., quinine sulphate  $\frac{1}{2}$  gr., fluid extract of belladonna root  $\frac{1}{2}$  m. in each tablet. *Dose.*—1 to 2 every two hours.

**Quininae Tannas (B.P., P. Helv. V, P.G. VI, P. Ned. V).**

*Dose.*— $1\frac{1}{2}$  to 15 grains (0.1 to 1 g.).

An amorphous yellowish-white powder, obtained by the decomposition of the sulphate with a solution of tannin. Contains from 30 to 35% of anhydrous quinine.

**Soluble** slightly in water and about 1 in 3 of alcohol 90%.

Being almost tasteless it is recommended for children, to be given in milk, but the slow dissociation in the intestines may be a disadvantage.

**Quininae Valerianas (B.P.C.).** (Termed "basic" in *Fr. Cx.* and *P. Ital. V*).  $C_{20}H_{24}O_2N_2 \cdot C_6H_5 \cdot COOH, H_2O = 444.3$ .

*Dose.*—1 to 3 grains (0.06 to 0.2 g.).

White crystals, or powder with slight valerianic odour. Contains not less than 71% of anhydrous quinine.

**Soluble** 1 in 120 of water, 1 in 2 of alcohol 90%.

**Pilulae Ferri Valerianatis Compositae (B.P.C.).** *Syn.* PILULAE TRIUM VALERIANATUM.

*Dose.*—1 or 2 pills. Contain 1 gr. each of the valerianates of iron, quinine and zinc. For nervous headache and hysteria. Have been found of value in paroxysmal sneezing.

**Cinchona Febrifuge.**

Originally this product consisted of the mixed alkaloids from *C. succirubra*. Owing to the cultivation of other species and of hybrids yielding more quinine, cinchona febrifuge has become a very variable product. For analyses of different samples, see J. A. Goodson and T. A. Henry, *Quart. J. Pharm.*, 1930, 238.

The following formula is said to be superior to any other in prophylaxis and superior to quinine in chronic cases of malarial fever as a remedial measure: Powdered cinchona febrifuge 10 gr., citric acid 20 gr., magnesium sulphate 20 gr., spirit of anise 10 m., syrup to  $\frac{1}{2}$  oz. *Dose.*— $\frac{1}{2}$  ounce 2 hours after meals.

In recent years *C. Ledgeriana* has been encouraged (to increase quinine production) at the expense of the other alkaloids. Recent samples of cinchona febrifuge suggest they have been made from *C. Ledgeriana* after the extraction of the quinine, and they contained greater amounts of amorphous alkaloids and quinidine. Although it is believed that cinchona alkaloids have equal anti-malarial action, it is important to have a definite standard.—*Brit. med. J.*, i/1930, 27.

Cinchona febrifuge has never attained any great popularity in India, and its consumption is on the decline.—*Brit. med. J.*, i/1933, 923.

**Quinetum (B.P.C.).**

*Dose.*—1 to 10 grains (0.06 to 0.6 g.).

As defined by the Malaria Commission of the League of Nations in 1931, it consists of a mixture of equal parts of quinine, cinchonidine and cinchonine, thus corresponding approximately to the

relative proportions of these alkaloids in the total alkaloids of red cinchona bark. It is more constant in composition than cinchona febrifuge and is given by mouth in the treatment of benign and malignant tertian malaria.

**Totaquina (B.P.).**

**Dose.**—1 to 10 grains (0.06 to 0.6 g.).

A nearly white, pale yellowish-grey, or pale brown powder consisting of a mixture of alkaloids. It contains not less than 70% of crystallisable cinchona alkaloids, of which not less than one-fifth is quinine.

**Soluble** almost completely in warm alcohol 95% and in chloroform; partially soluble in ether, benzene and light petroleum; almost insoluble in water.

Field trials carried out under the auspices of the Health Organisation of the League of Nations in Rumania, Nanking, Kuala Lumpur, and other places, show that totaquina acts like quinine as a potent remedy in all forms of malaria. As this was not a carefully controlled experiment, however, it is not possible to decide from it whether totaquina is a little better than quinine or not quite so good. Two types of totaquina were used in the tests, Type I, made direct from the bark of *C. succirubra*, and Type II, made from residues of quinine extraction and adjusted to the Malaria Commission's standard specification. The observations made at the different centres were not sufficiently precise and unanimous to warrant a final decision on the relative merits of the different samples.—E. J. Pampana and William Fletcher, *Quart. Bull. Hlth Org., L. o. N., Sept., 1934*.

The Malaria Commission, as a result of these experiments and Dr. Fletcher's Report, considered that "Totaquina seems able to fulfil the purpose for which it was intended, since, having regard to its efficacy—equal to or only slightly less than that of quinine—facility of preparation and cost price, its use would enable malaria treatment to be extended over a wider field."—*Quart. Bull. Hlth Org., L. o. N., Sept., 1934*.

Adult male prisoners in Lahore who were suffering from malaria were treated with quinine and totaquina, types I and II, in strict rotation, according to the method recommended by the League of Nations. In benign and malignant tertian malaria there was no distinct difference in efficacy between quinine and the two types of totaquina in causing the disappearance of parasites and fever. The evidence as to toxicity was not very reliable. It failed to show any significant difference in toxicity between quinine and the two types of totaquina.—E. P. Hicks and S. D. Chand, *Indian med. Gaz., 1935, 579*.

From clinical tests, using an experimental batch of Philippine totaquina in doses of 0.6 g. three times daily, it is concluded that the combination is about equal to quinine sulphate in its therapeutic effect. It does not destroy the crescents of subtertian malaria, being similar in this respect to quinine and Atebrin, but schizonts and gametocytes of benign tertian disappear in two to three days. Addition of Plasmoquine to the treatment clears the blood of crescents. No untoward effects were observed.—Marañon, Perez and Russell, *Philipp. J. Sci., 1935, 56, 231*.

The treatment of a large series of cases of benign and malignant tertian malaria with totaquina II and with quinine has shown that these two drugs are about equal in clinical value. It proved to be no more toxic, while its cost is about half that of quinine hydrochloride and three-quarters that of quinine

sulphate. Totaquina is thus an effective anti-malarial remedy and can be safely substituted for quinine with a consequent considerable saving in expenditure.—A. N. Kingsbury, *Rep. Inst. med. Res., F.M.S., 1937, 4.*

**Pamaquina.** *Syn. and Prop. Names.* BEPROCHIN, PLASMOCHIN, PLASMOQUINE (Bayer Products, London), PRÆQUINE (Pharmaceutical Specialities (May & Baker) Ltd., London).

$C_{19}H_{29}ON_3 = 315.45$ .

*Dose.*— $\frac{1}{8}$  grain (0.01 g.).

Pamaquin is a synthetic antimalarial substance consisting of N-( $\omega$ -diethylamino- $\alpha$ -methylbutylamino)-6-methoxyquinoline. It occurs as a pale yellow, granular powder.

**Insoluble** in water; readily soluble in alcohol.

**Uses.** Pamaquin is used either alone or, more frequently, in combination with quinine (or mepacrine hydrochloride, *q.v.*). Its antimalarial action is the reverse of quinine in that it acts more powerfully on the gametocytes than on the schizonts. It is most effective in benign tertian and quartan malaria, but is less efficient than quinine in subtertian infection. A combination of the two drugs is therefore the ideal procedure, and a dosage of 0.01 g. of pamaquin and 0.125 g. of quinine three times daily for a week is usually effective in curing tertian and quartan malaria, and relapses are said not to occur so frequently as with quinine. Owing to its action in destroying the gametocytes of all types of malaria it is of particular value as a prophylactic and it reduces the danger of conveying infection. The use of pamaquin is especially indicated in quinine idiosyncrasy, in blackwater fever, and in malaria in pregnancy. The drug is usually well tolerated, especially by children, but large doses may give rise to cyanosis, epigastric pains and methæmoglobinuria. It is best taken after meals, and it is advisable not to exceed a dose of 0.06 g. daily.

Plasmoquine assists malariologists as follows: (1) In minute doses given to gametocyte carriers prevents infection of mosquitoes. (2) In dose of 0.06 g. spread over a week it removes gametocytes from the blood. (3) In somewhat larger doses it prevents infection after injection of sporozoites. (4) In 2 treatments (0.06 g. over a week) it prevents relapses, reduces number of carriers, and so reduces number of infections.

Badly infected estates in Ceylon in which antilarval measures were impossible kept practically free from malaria for more than two years by anti-gametocyte dosing with Plasmoquine.—Lt.-Col. W. W. Clemesha, *Lancet*, 1/1932, 750.

There is no satisfactory drug in existence which, taken in therapeutic doses, will prevent contraction of malaria after bites from infected mosquitoes. Plasmoquine in maximum therapeutic doses can be tolerated for 8 days or more and has the same effect as a true causal prophylactic should have, but as the prophylactic dose is too near the toxic dose to be safely taken for more than a few days it is of little value in the prevention of malaria. Plasmoquine, either alone or in combination with quinine, is not recommended for the treatment of malaria. Small doses (0.02 g.) have little or no curative action on asexual forms of the malarial parasites and daily doses of 0.06 to 0.08 g. may cause cyanosis, fatigue, profuse perspiration, or cardiac symptoms.—Col. S. P. James, Health Organisation of the League of Nations, *Brit. med. J.*, ii/1933, 928.

It is admitted that, with a daily dosage of 0.06 g. or over, toxic symptoms are of common occurrence, but with the smaller doses which are in common use for the routine treatment of malaria, *e.g.* 0.015 g., severe toxic complications are of comparatively rare occurrence. Unable to agree with the findings of the Malaria Commission that the combined quinine and Plasmoquine treatment for benign tertian malaria is "of doubtful value." If one is to condemn the use of

this valuable drug, Plasmoquine, because of a relatively small number of cases of serious results often due to improper individual dosage or supervision, one should equally condemn many of the new arsenical preparations used in the treatment of syphilis and other diseases.—J. A. Sinton, *Quart. Bull. Hith Org., L.o.N.*, 1935, 657.

The prophylactic value of quinine rather doubted by Army experts; evidence in favour of Plasmoquine obtained, but lower doses ineffective and toxicity of higher doses led to doubts as to use on large scale. As a therapeutic agent, however, it established its position during 1932, the average relapse rate during 1927-31 being 277 per 1000 and for 1932 in Plasmoquine-treated patients 20 to 47 per 1000.—Army Health Rept. 1932, *Brit. med. J.*, i/1934, 253.

**Quino-Plasmoquine** (*Bayer Products, London*). *Syn.* QUINO-BEPROCHIN.

A preparation of Plasmoquine and quinine sulphate, in tablets containing Plasmoquine 0.01 g. and quinine sulphate 0.3 g.

**Uses.** The insufficient action of Plasmoquine on the ring forms and schizonts of subtertian malaria led to the use of this combination, which has now largely replaced the use of Plasmoquine alone. For the treatment of all types of malaria, especially subtertian, from 3 to 4 tablets are given daily and a complete cure may be expected within 2 or 3 weeks.

**Plasmoquine Compound** (*Bayer Products, London*). This is a similar combination to Quino-Plasmoquine, but with a smaller dosage of quinine (tablets contain 0.01 g. Plasmoquine and 0.125 g. quinine sulphate). It is used similarly to Quino-Plasmoquine.

**Mepacrinæ Hydrochloridum** (*B.P. Add. III*).

*Syn. and Prop. Names.* ATABRIN, CHINACRIN, ERION, ATEBRIN (*Bayer Products, London*), QUINACRINE (*Pharmaceutical Specialities (May & Baker) Ltd., London*).

$C_{23}H_{30}ON_3Cl, 2HCl, 2H_2O = 508.7$ .

**Dose.**— $\frac{1}{4}$  to  $1\frac{1}{2}$  grains (0.05 to 0.1 g.). (*B.P. Add. III* gives the metric dose incorrectly as 0.05 to 1.0 g.).

The dihydrochloride of 2-chloro-5-( $\omega$ -diethylamino- $\alpha$ -methylbutylamino)-7-methoxyacridine, prepared synthetically. It is a yellow, crystalline powder with a bitter taste.

**Soluble** 1 in about 30 of water, giving a neutral solution; also soluble in alcohol.

**Stability in Solution.** Aqueous solutions undergo hydrolysis especially when heated. The cyclical component, 2-methoxy-6-chloroacridone, is precipitated as a yellow crystalline powder. Injections should be given as soon as possible after preparation, and aqueous solutions for oral administration should be given not later than 12 hours after preparation.—F. Mietzsch, H. Mauss and G. Hecht, *Indian med. Gaz.*, 1936, 521.

**Uses.** Mepacrine hydrochloride has a specific parasitotropic action in malaria. It affects both the gametocytes and the schizonts in tertian and quartan malaria, but acts only on schizonts in subtertian malaria, in which condition it is best given in association with pamaquin. The advantages claimed for mepacrine hydrochloride are that its action is prompt, it is pleasant to take, its toxicity is low, and relapses are rare. It is well tolerated by children and pregnant women and is of value in blackwater fever and quinine idiosyncrasy. Most cases of malaria are cured within a week, and a daily dose of 0.1 g. is stated to be more effective in keeping infected persons free from fever than a daily dose of 5 gr.

of quinine. In ordinary therapeutic doses it does not usually give rise to toxic symptoms, but with comparatively large doses there may be epigastric pain, mild diarrhoea, and a yellow discoloration of the skin and conjunctiva. The discoloration, which disappears within a week or two, is not due to jaundice but to delayed excretion of the drug through the skin.

In a daily dose of 1 tablet (0.1 g.) is effective as a clinical prophylactic but cannot ordinarily be used for the purpose as even this small dose quickly colours the skin yellow. It is, however, as efficient as quinine in the control of malarial paroxysms, and in cases with severe vomiting or other malignant symptoms, may be given intravenously or intramuscularly, a suitable dose intravenously being 0.3 g. in 5 ml. normal saline.—Col. S. P. James, Health Organisation of the League of Nations, *Brit. med. J.*, ii/1933, 928.

Signs of toxicity observed in Europeans were headache in one case and abdominal pain (responding to diet and alkalis) in 12% of cases. A combination of Atebrin and Plasmoquine more toxic than Atebrin alone and should never be used in the febrile stage of subtertian malaria. Relapse rate reduced from 60 to 43%, and treatment beyond 5 days probably does not lessen tendency to relapse, 1.5 g. being the optimum adult dose.—P. D. Johnson, *Brit. med. J.*, i/1934, 473. See also E. J. R. MacMahon, *ibid.*, 477.

In subtertian malaria it is necessary to give a 5-days course of Plasmoquine in addition. Results so favourable that Atebrin and not quinine is now the drug in ordinary use for the treatment of malaria on estates served by the Malacca Agricultural Medical Board (Straits Settlements).—A. L. Hoops, *Brit. med. J.*, i/1933, 993.

To-day it is justifiable to regard Atebrin as an anti-schizont remedy the value of which has been established in practice and with which a successful course of treatment can be carried out in a remarkably short space of time.—F. M. Peter, *Trans. R. Soc. trop. Med. Hyg.*, 1935, 50.

Atebrin is the best drug available for the controlled treatment of all types of malaria in Malaya, where effective oral administration is preferable to injection.—A. L. Hoops, *Trans. R. Soc. trop. Med. Hyg.*, 1935, 249.

Mass treatment with Atebrin was given to labour forces on several malarial areas in Malaya. Atebrin was given in varying doses for periods up to four months without any apparent ill-effects and without upsetting the labour forces. No serious toxic effects such as mental symptoms were seen amongst the many thousands of coolies treated. A certain number of cases of colic occurred—approximately 3%.—R. B. Wallace, *J. trop. Med. (Hyg.)*, 1936, 39.

As the result of an investigation carried out over the past three years, the Malaria Research Division of the F.M.S. reports that the smallest effective quantity of Atebrin for the control of clinical malaria in adults is 0.3 g. given as a single dose at weekly intervals.—A. N. Kingsbury, *Rep. Inst. med. Res., F.M.S.*, 1937, 4.

**Atebrin Psychosis.** Earliest symptoms are mental exhilaration and insomnia controlled only by drastic sedatives. This is soon followed by unrest and continuous and uncontrollable verbosity which progresses until the patient is walking the floor and almost shrieking, the language being coherent and usually an elaboration of some recent experience. The patient lashes out at surrounding objects or at those attempting restraint. This condition merges into a somnolent delirium. On regaining consciousness there is mental confusion with complete disorientation. This may clear up in a few days or become chronic.—C. C. Turner, *per Trop. Dis. Bull.*, 1937, 151.

**Comparison of Atebrin and Quinine for Prophylaxis.**—Observations were made for varying periods up to one year on 1253 individuals on two malarious plantations in Selangor, Federated Malay States, the predominant parasites on the estates being, respectively, *P. vivax* and *P. falciparum*. One group received 0.2 g. of Atebrin on each of two successive days each week, another group received 0.4 g. of quinine dihydrochloride daily (the dosage quoted is that for adults), and a third group as a control received a coloured tablet. Prophylactic treatment, both with Atebrin and with quinine, effected a marked reduction in the number of attacks, the Atebrin being somewhat more potent than the quinine. When administration of the drugs was suspended there was a rapid return of the clinical signs of malaria, and it was suggested that this post-prophylaxis malaria was due to the reappearance of infections which had been clinically

and histologically hidden during treatment, the action of the drugs being, in effect, to prolong the incubation period. While the complete safety of prolonged Atebrin administration was not definitely proved, it appeared that the risks are not of a high order.—J. W. Field, J. C. Niven and E. P. Hodgkin, *Bull. Hlth Org. L.o.N.*, 1937, 236.

**LAMBLLIA INFECTIONS.** The good therapeutic results obtained in the treatment of lamblia infections of the intestine by the oral administration of Atebrin have been verified by a number of workers. The dosage consists of 0.1 g. three times daily only, if necessary, after food for five days. It may also be employed as a vaginal douche to get rid of *Trichomonas vaginalis*.—N. H. Fairley, *Practitioner*, ii/1939, 500.

Atebrin has a specific action in the eradication of giardia infections. Abstracts of numerous papers to this effect.—*Trop. Dis. Bull.*, 1940, 377.

**ORIENTAL SORE.** Solution of Atebrin injected into the skin round oriental sores quickly destroys the parasites and cures the disease. The dose administered at one sitting commences at 0.05 to 0.1 g. in 1 or 2 ml. of distilled water, and is increased at subsequent sittings to 0.3 g. In some cases only a single injection is required to bring about a cure.—F. Flarer, *Trop. Dis. Bull.*, 1939, 454.

### **Mepacrinæ Methanosulphonas (B.P. Add. III).**

**Prop. Names.** ATEBRIN MUSONAT (Bayer Products, London), QUINACRINE SOLUBLE (Pharmaceutical Specialities (May & Baker) Ltd., London).  $C_{23}H_{30}ON_3Cl, 2CH_3SO_3H = 591.9$ .

**Dose.**— $\frac{3}{4}$  to  $1\frac{1}{2}$  grains (0.05 to 0.1 g.), by intramuscular injection.

The dimethanesulphonate of mepacrine, a yellow crystalline substance with a bitter taste.

**Soluble** 1 in 3 of water and 1 in 36 of alcohol 95%.

**Uses.** As for mepacrine hydrochloride, but is especially indicated where there is an abnormally large invasion of parasites and severe complications. It is best given intramuscularly, but if given intravenously the single dose of 0.1 g. should not be exceeded and the injection should be given very slowly. This dose should be dissolved, when required for use, in 3 ml. of sterile distilled water. Solutions must not be heated or stored for any length of time.

Death following intramuscular injection. It seems difficult to be certain beforehand whether a patient will react badly to Atebrin, and also difficult to increase its excretion once a full therapeutic dose has been injected.—P. B. Fernando and E. M. Wijerama, *Lancet*, ii/1935, 1056.

Among adults, pregnant women have been found particularly liable to collapse after injections. Convulsions due to malaria were of frequent occurrence among children in the early stages of the epidemic. Convulsions occurring a few minutes or hours after an Atebrin injection and attributed to the Atebrin injection have occurred in both children and adults. They were always fatal.—R. Briercliffe, Report on the Malaria Epidemic in Ceylon, per *Lancet*, ii/1935, 1078.

Two intramuscular injections of 0.375 g. at an interval of 24 hours brought the temperature down in the majority of cases and caused disappearance of the asexual stages of the parasites (whether *P. vivax* or *P. falciparum*) as a rule within 3 days. Ill-nourished children are likely to collapse shortly after the injection, with vomiting, giddiness and fainting. Unable to arrive at the conclusion that treatment with Atebrin Musonate is in any way superior to that of quinine as regards immediate effects, though the injections are painless.—S. Somasundram, *Trans. R. Soc. trop. Med. Hyg.*, 1935, 104.

Owing to the very slow excretion or destruction of Atebrin in the body it seems unnecessary to exceed for intravenous injection the dose of 0.1 g., for an adult. The margin of safety is probably not great and intravenous injection should be resorted to only in emergency. The injections should be made very slowly and timed to take several minutes for completion. The total injection over a period of twenty-four hours should not exceed 0.3 g.

Untoward effects of Atebrin appear to include: gasping or accelerated respiration, circulatory failure, collapse, vomiting, possibly rise of temperature,

psychoses, loss of appetite and of weight, abdominal pain, headache, diarrhoea, yellowed sclera, rather persistent yellowing of the skin.

In view of the very slow excretion or destruction of the drug in the body, it is reasonable to consider that a course of treatment with it should not be repeated within a period of, say, eight weeks, and that the drug should be taken under supervision of a physician.—W. T. Dawson, W. Gingrich, and E. D. Hollar, *Amer. J. trop. Med.*, 1935, 15, 515.

There were no toxic symptoms following intravenous or intramuscular injection in 34 cases, and inadvertent escape of the solution into the subcutaneous tissues caused no inflammation. As far as can be judged from a small series of cases, Atebrin Musonate is better given intramuscularly, and three daily doses or possibly four appear to be adequate. It may be necessary to revise this opinion if it is found that larger doses can be safely given intravenously. The cost of three intramuscular doses of Atebrin Musonate, 0.375 g. each, is four times that of 1 ounce of quinine or of a course of 15 tablets of Atebrin dihydrochloride. Atebrin Musonate would thus be uneconomical for routine use in natives, but the slight inconvenience involved and lack of all unpleasant toxic symptoms, make it a strong rival to quinine and oral Atebrin for patients able to bear the expense.—J. A. Carman and R. P. Cormack, *Trans. R. Soc. trop. Med. Hyg.*, Jan., 1936, 395.

**Atebrin Compound** ("ATEPE") (*Bayer Products, London*). Tablets containing 0.1 g. of Atebrin and 0.005 g. of Plasmoquine, the dose for adults being 3 tablets daily for 5 to 7 days, and as a prophylactic 4 tablets per week.

**Certuna** (*Bayer Products, London*). Dimethyl-amino-oxyquinolyl-amino-butane. A preparation with a specific action on the crescents of *Plasmodium falciparum* (subtertian malaria), for use either alone or in combination with Atebrin. It is available in tablets of 0.02 g. *Dose*.—For the treatment of the malarial attack Certuna should be combined with Atebrin, the Atebrin doses of 0.3 g. given for 5 to 7 days being supplemented by daily doses of 0.03 to 0.06 g. Certuna, which can be given at once or divided into three separate doses. Administration for three consecutive days gives good results, but the doses may be continued for 6 to 7 days. Prophylactically, a dose of 0.06 g. Certuna exerts a sufficient damaging effect on the crescents.

Of value as a gametocide in malignant tertian malaria. In doses of 0.02 g. daily for 5 days it produced no toxic signs. In severe cases it is recommended to give injections of 0.3 g. of Atebrin followed by oral Atebrin (0.1 g. thrice daily) for 4 days or more. When temperature has dropped to normal and there are crescents in the blood give 0.01 g. Certuna with 0.1 g. Atebrin thrice daily. When crescents are numerous 0.02 g. of Certuna may be given. Crescents cease to flagellate on the second day of administration, and disappear in from 4 to 7 days.—P. Muhlsens, *Dtsch. med. Wschr.*, i/1938, 295.

Therapeutically inferior to Plasmoquine in malignant tertian malaria, but has marked gametocidal powers.—W. Kikuth, *Klin. Wschr.*, 1938, 17, 524.

**Cupreæ Cortex.** The bark of *Remijia pedunculata* and other species. Contains the alkaloid cupreine,  $C_{19}H_{29}O_2N_2 = 312.2$ , which is allied to quinine, and also about 2 to 3% of quinine. Cupreine salts have been employed similarly to the salts of quinine. It can be converted into quinine by treating with sodium in methyl alcohol solution and heating the solution with methyl iodide.

**Æthylhydrocupreina.** *Syn. and Prop. Name.* OPTOCHIN (*Howards, Ilford*), NUMOQUIN.  $C_{21}H_{29}O_2N_2 = 340.2$ .

*Dose*.—4 grains (0.25 g.). This dose is given every five hours, day and night, for three days only, and five ounces of milk is given with every dose. For children the dose is very much less; e.g., for a 2-year old child, one-seventh the adult dose.

A minutely crystalline powder with bitter taste, prepared synthetically from quinine by hydrogenation, demethylation to hydrocupreine and subsequent ethylation.

Almost *insoluble* in water, soluble in alcohol, ether, chloroform and dilute acids.

**Uses.** Has a very potent bactericidal action against all types of pneumococcus, and is employed in the treatment of pneumonia, treatment being commenced immediately on diagnosis. In spite of its undoubted pneumococcicidal action, the fact that the therapeutic dose is so near the toxic dose necessitates extreme care in its administration and limits its usefulness, though it has been widely employed on the Continent and in America. If auditory or visual disturbances develop during treatment it should be immediately suspended. It is important to note that *only the base* is employed in pneumonia, the hydrochloride being too toxic for internal use.

Amaurosis following ingestion of a total of 58 grains of ethylhydrocupreine over 3 days.—B. Alvis, *J. Amer. med. Ass.*, ii/1929, 1253.

An average mortality of 25% for bronchopneumonia in children contrasted with a consecutive series of 44 cases treated with Optochin without a single death.—*Brit. med. J.*, i/1933, 968.

**Æthylhydrocupreinae Hydrochloridum** (B.P.C., *P. Helv. V. P. Ned. V.*).  
*Prop. Name.* OPTOCHIN HYDROCHLORIDE (*Howards, Ilford*).  $C_{21}H_{25}O_2N_3.HCl$   
= 376.7.

A white crystalline powder soluble in water about 1 in 4.

**Uses.** This is not now employed internally, since its too rapid absorption is liable to give rise to grave visual disturbances. It is used locally in 1 or 2% solution in eye affections especially in pneumococcal infections and as a prophylactic against infection in laceration of the cornea. Its use is at first painful, but anaesthesia is produced in 2 to 30 seconds.

Ulcus corneae serpens has been treated with a 1% ointment (made with the base) or a 1% or 2% solution. A pad of sterile wool or gauze is soaked in the solution and then left on the ulcer for 5 or 10 minutes. After this the 1% solution is *instilled* into the eye every hour or so during the day, or the ointment applied 5 to 6 times *per diem*. *Note.*—Solutions should be freshly prepared. They decrease in efficiency after 3 or 4 days.

In gonorrhoeal conjunctivitis and photophobia accompanying eczematous conjunctivitis, scrofular ophthalmia, and keratitis, has also proved useful.

**PNEUMOCOCCAL CONJUNCTIVITIS.** Used in a 1% solution, it rapidly frees the conjunctival sac of infection, but its use over long periods is not to be recommended as it sometimes has a deleterious effect on the cornea.—R. H. B. Barrow, *Med. Pr.*, ii/1936, 550.

**Octylhydrocupreinae Dihydrochloridum** is the *isooctyl* compound. A 0.5 to 1% solution has been used as a disinfectant for wounds.

**Peganum** (B.P.C.). The dried seeds of *P. Harmala* (Rutaceae). Contains the alkaloids harmaline and harmine. Banisterine from *Banisteria Caapi* is an alkaloid identical, chemically and pharmacologically, with harmine.

These alkaloids, and their derivatives, harmol and harmalol, have been employed in the symptomatic treatment of parkinsonism, but are stated to be of less value than hyoscine.

The alkaloid of *Banisteria Caapi* was compared directly with that of *Peganum harmala*, which is harmine, by analysis, preparation of derivatives, ultraviolet absorption spectra, and biological experiments. They are undoubtedly identical, and therefore the previously proposed names of telepathine, yajaine and banisterine for the same alkaloid should be dismissed. In mice and rabbits a limited detoxication of harmine by Sodium Amytal has been demonstrated.—A. L. Chen and K. K. Chen, *Quart. J. Pharm.*, 1939, 30.



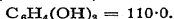
**Picrorhiza** (B.P.C.). *Dose*.—10 to 60 grains (0.6 to 4 g.). The dried rhizome of *P. Kurroa* (Scrophulariaceæ). Tonic, antiperiodic, aperient. This and *Amphicome Emodi* are called Kaur.

**Extractum Picrorhizæ Liquidum**. *Dose*.—15 to 60 minims. 1 in 1 of alcohol 60%.

**Tinctura Picrorhizæ**. *Dose*.— $\frac{1}{2}$  to 1 drachm. 1 in 4 of alcohol 45%.

## RESORCINOL

*B.P., U.S.P. XI, P. Helv. V, etc.*



*Syn.* RESORCINUM (*Fr. Cx.*), RESORCIN, *m*-DIHYDROXYBENZENE.

*Dose*.—1 to 5 grains (0.06 to 0.3 g.). *U.S.P. XI* average dose 2 grains. *Fr. Cx.* has max. single dose 8 gr.

White crystalline plates or powder, melting at 110° to 111°, and easily volatilised. Preserve from light.

**Soluble** 1 in 1 of water, 1 in 1 of alcohol 90%, 1 in 20 of olive oil, 1 in 1 of ether, 1 in 1 of glycerin; very slightly soluble in chloroform, carbon disulphide and benzene.

**Incompatible** with spirit of nitrous ether and caustic alkalis.

**Uses.** Resorcinol was formerly used internally as an antipyretic, but the action is too short to be useful and there is a danger of the formation of methæmoglobin. It has a marked antiseptic action and is employed externally in solution or as ointment in the treatment of various skin diseases. A 1 in 4 solution in glycerin is excellent for removing epidermic scales in chronic skin diseases and for eliminating scurf of the scalp, and a 2% ointment is of value in the scaly stage of eczema and in sycosis barbæ. Stimulating hair lotions, such as Spiritus Resorcinolis, are beneficial in the treatment of dandruff and alopecia, but they should not be used on fair hair, and before use it is important to free the hair from soap and alkali to avoid discoloration. Epithelioma and rodent ulcer have been treated with ointments and plaster up to 30% strength, and it may be applied locally to condylomata and mucous patches. It should be remembered, however, that resorcinol is dangerous when applied over large surfaces, especially when used in strong preparations.

A 5% solution may be injected into the bladder, without causing any irritation, in inflammatory affections of this organ, likewise in vesical catarrh after gonorrhœa; 5 to 10% solution is of service also in syphilitic sores. A 1% solution is useful as an eye lotion in conjunctivitis.

**Gargarisma Resorcini** (*P.E.H.C.*).

Resorcinol 15 grains, glycerin 1 dr., water to 1 oz.

**Aurist. Resorcinol.** (*N.I.F.*). Resorcinol 5 gr., industrial methylated spirit 6 dr., water to 1 oz.

[P1] **Lotio Excitans** (*St. G. H.*). Resorcinol 5 gr., mercuric chloride  $\frac{1}{2}$  gr., glacial acetic acid 3 m., chloral hydrate 10 gr., tincture of cantharides 20 m., alcohol 60% to 1 oz. For the scalp.

[P2] **Lotio Resorcinolis Composita** (*Mid. H.*). Resorcinol 5 gr., mercuric chloride  $\frac{1}{2}$  gr., castor oil 15 m., tincture of quillaia 7½ m., spirit of rosemary 30 m., mucilage of tragacanth 15 m., water to 1 oz. A stimulating application for pityriasis of the scalp. *St. M. H.* has resorcinol 10 gr., industrial methylated spirit 1 dr., water to 1 oz.

[P1] **Lotio Resorcinolis Pilocarpinae et Cantharidini.**

Resorcinol 80 gr., pilocarpine hydrochloride 15 gr., solution of cantharidin 1½ oz., tincture of capsicum 4 dr., spirit of camphor 6 dr., castor oil 10 to 60 m., oil of lavender 30 m., alcohol 90% to 8 oz. A useful stimulating lotion in alopecia prematura for use after exfoliative treatment.

**Pasta Resorcinolis** (*B.P.C.*). *Syn.* LASSAR'S STRONGER RESORCIN PASTE.

Resorcinol, zinc oxide and starch, of each about 20% with liquid paraffin.

**Pasta Resorcinolis Mitis** (*B.P.C.*). *Syn.* LASSAR'S MILD RESORCIN PASTE.

Resorcinol about 10%, zinc oxide and starch, of each about 25%, with liquid paraffin.

**Spiritus Resorcinolis** (*B.P.C.*). *Syn.* LOTIO RESORCINOLIS COMPOSITUS, SPIRITUS CAPILLARIS.

Resorcinol and castor oil of each 1 in 40 in Cologne spirit and alcohol.

**Unguentum Resorcinolis** (*B.P.C.*). 12½% in glycerin, wool fat and white soft paraffin. *R.L.O.H.* has resorcinol 4 gr., yellow soft paraffin to 1 oz.

**Unguentum Resorcinolis Compositum** (*B.P.C.*). Resorcinol 4%, bismuth subnitrate 8%, with water, starch, zinc oxide, birch tar oil and potassium pyrosulphite in wool fat, ceresin and yellow soft paraffin.

**Unguentum Resorcini Compositum** (*St.J.H.*). *Syn.* IHLE'S PASTE.

Resorcinol, zinc oxide, starch, of each 22 gr. in soft paraffin to 480 gr.

**Unguentum Resorcinolis et Acidi Salicylici.** *Syn.* CASTELLANI'S OINTMENT. Resorcinol 60 gr., salicylic acid 10 gr., lanolin and soft paraffin to 1 oz.

The most popular remedy for Dhobie itch in Africa and Asia.

**Unguentum Resorcinolis et Bismuthi Compositum** (*B.P.C.*). Resorcinol and bismuth subchloride of each 8%, with water, zinc oxide, starch, birch tar oil, oil of cade, and wool fat.

**Ruscoin** (*Evans, Sons, Lescher & Webb, Liverpool*). Ointment containing resorcinol, oil of cade, zinc oxide, etc., in a lanolin base. Eczema, hæmorrhoids, etc.

**Resorcinolis Monoacetat.** *Syn. and Prop. Name.* RESORCIN MONACETATE, EURESOL (*Knoll, London*).

A reddish-yellow, viscous liquid. Dissolves 10 to 30% in acetone, for use in acne, seborrhœa and sycosis. Euresol pro Capillis has perfume added.

**Lotio Resorcinol Monoacetatis Compositum** (*B.V.H.*). Solution of resorcinol monoacetate (1 in 2 in acetone) 2 dr., solution of formic acid (25%) 10 m., spirit of rosemary 1 dr., sodium taurocholate 2 gr., water to 6 oz.

**Hexyl-Resorcinol** (*B.P.C.*). *Syn.* 1 : 3-DIHYDROXY-4-HEXYLBENZENE, 4-*n*-HEXYLRESORCINOL.  $C_6H_3(OH)_2 \cdot (CH_2)_5 \cdot CH_3 = 194.1$ .

*Dose.*—2 to 10 grains (0.12 to 0.6 g.) thrice daily.

**Patents.** The manufacture of hexyl-resorcinol and allied compounds is covered by a number of British patents dating from 1923, owned by American manufacturers. In 1927 they were the subject of an action in the Courts. Details in 19th Edn., p. 753.

Stable white crystals with pungent odour and astringent taste, m.p. not below 66°.

**Soluble** 1 in 2000 of water, readily in ether, chloroform and alcohol and in oils.

**Uses.** A germicide, especially for gram-positive organisms, the phenol coefficient ranging from 46 to 52. Its power is retained in both acid and alkaline urine even in high dilution. Given by the mouth, the compound is secreted in the urine at a rate producing continuous action in the urinary tract. Gelatin capsules containing 0.15 g. in 25% olive oil solution are taken *immediately after* each meal thrice daily, 3 to 4 being taken on each occasion. Chronic *B. coli* infections and *Staphylococcus* infections have been treated with it; it acts best in early cases. Pyelitis and cystitis caused by organisms other than *B. coli* are cleared up in a few weeks. *B. coli* infections require, on the average, about as many months. It has now been largely superseded in the treatment of urinary tract infections by mandelic acid or sulphonamide therapy.

Hexyl-resorcinol is an effective anthelmintic for roundworms, hookworms and threadworms. The dose is 0.5 g. for a child and 1 g. for an adult, given in hard gelatin capsules first thing in the morning on an empty stomach. No food is taken for four or five hours, and a purge of magnesium sulphate is given the following morning.

Externally, a solution of hexyl-resorcinol 1 in a mixture of glycerin 300 and water 700 is used as a disinfectant for the skin and mucous membrane.

**ROUNDWORM.** Possibly the most effective substance known against ascaris, well over 90% being removed in over 1000 cases. Its disadvantages are that it combines with protein and is relatively ineffective if taken when food is present in the stomach or intestines, that it causes a certain amount of irritation in the stomach, and that the crystals, unless protected in some way, may cause local "burns" of the mucous membrane of the mouth—it is best given in sugar-coated pills, with instructions that they should not be chewed.—P. D. Lamson and co-workers, *J. Amer. med. Ass.*, ii/1932, 294.

**HOOKWORM.** No attempt has been traced at evaluation of hexyl-resorcinol through deworming. The drug has hitherto caused no deaths. Relative success depends on starvation, rigorous to a degree required for no other anthelmintic. Encapsulation of the drug shifts to the invisible stomach the ugly necrosis it causes, but aesthetic gain need be no more than a decent shrouding of pathological damage. Hope of its usefulness on a mass scale is slight.—C. Lane, *Lancet*, i/1935, 1463.

**THREADWORM.** Santonin is unsatisfactory. Better results are obtained with hexyl-resorcinol administered as an enema in a 1 in 2000 solution immediately after an evacuation brought about by an ordinary soap and water enema. A quart of the solution is given to adults and as much as can be retained to children. The minimum routine necessary to bring about cure consists in the administration of an enema every other night at bedtime over a period of at least three to four weeks. There is no satisfactory alternative to the enema.—W. H. Wright *et al.*, *Publ. Hlth Rep.*, Wash., 1939, 2005.

**Emulsio Hexyl-Resorcinoli** (*Gl. Orm. H.*). (Dose for 1 year old child.) Hexyl-resorcinol 1 gr., olive oil 10 m., acacia 2½ gr., chloroform water to 1 drachm.

**Caprokol** (*British Drug Houses, London; Sharp & Dohme, London*) is a solution of hexyl-resorcinol in olive oil. In capsules containing 0.15 g. of hexyl-resorcinol or as a 2½% solution.

**Hexylresorcinol Solution S.T. 37** (*Sharp & Dohme, London*). A solution of hexyl-resorcinol of low surface tension (37 dynes per sq. cm.) and high bactericidal activity. Used undiluted for cuts, infected wounds, abscesses, etc., and diluted with 1 to 3 parts of water as a mouthwash or gargle.

**Lubisan** (*Bayer Products, London*). Resorcin-monoethyl-etherdiethyl-carbonate in perles containing 0.15 g. For oxyuriasis in children. *Dose*.—2 to 6 perles daily. A granulate is prepared for administration to infants who cannot swallow.

**Permfoam** (*Gilmont Products, London*). Foaming contraceptive consisting of two jellies kept separate in a double tube until required for use. One jelly is acid, containing citric acid, boric acid and saponin in a non-greasy base. The second jelly contains sodium bicarbonate with hexylresorcinol as spermicide and egg albumen as foam stabiliser.

**Prentif Suppositories** (*Prentif Ltd., London*). Contraceptive suppositories in which hexyl-resorcinol is the spermicidal ingredient in an acid gelatin base of pH 2.2. **Prensols** are the same, but smaller, for use with a cervical cap.

**Heptylresorcinol.** *Syn. and Prop. Name.* 2-4 DIHYDROXY-PHENYL-*n*-HEPTANE, DIHYDRANOL (*Sharp & Dohme, London*).

*Dose*.—5 to 15 grains (0.3 to 1 g.) usually given in hard gelatin capsules containing 0.15 g. in olive oil.

A powerful germicidal substance possessing selective action against the putrefactive flora of the intestinal tract. It has also been employed as an anthelmintic and in amoebiasis.

## RHEUM

*B.P., U.S.P. XI, P. Helv. V, Fr. Cx., etc.*

*Syn. RHEI RHIZOMA.*

*Dose*.—3 to 15 grains (0.2 to 1 g.).

The rhizome (*U.S.P. XI*, rhizome and roots), partially decorticated and dried, of *Rheum palmatum* and other species of *Rheum* (*Polygonaceæ*), except *R. rhaponticum*, grown in China and Tibet and known in commerce as Shensi, Canton or high-dried rhubarb.

**Uses.** Rhubarb is employed as a stomachic in atonic dyspepsia and as a laxative. It is useful in diarrhoea, since the tannin present exerts an astringent action after purgation has affected removal of irritant substances. It is not advisable, however, for continued use in chronic constipation.

A mixture consisting of compound rhubarb powder 1 oz., and chloroform water to 2 oz., causes rapid disappearance of symptoms in bacillary dysentery in children, but is of no use in adults. (*Dose*.—1 teaspoonful every 2 hours for a child of two years.) Acute bacillary dysentery in adults has been effectively treated by half a teaspoonful of powdered rhubarb in cachets every 1, 2, or 3 hours.

**Extractum Rhei** (*B.P.C.*).

*Dose*.—2 to 8 grains (0.12 to 0.5 g.).

A dry extract prepared with alcohol 60%.

**Extractum Rhei** (U.S.P. XI). *Average dose.*—8 grains (0.5 g.).  
1 g. represents 2 g. of rhubarb.

**Extractum Rhei Liquidum** (B.P.C.).

*Dose.*—10 to 30 minims (0.6 to 2 ml.). 1 in 1.

**Infusum Rhei Concentratum** (B.P.C.).

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.). 1 in 2 $\frac{1}{2}$ .

Is 8 times the strength of the fresh infusion.

**Infusum Rhei Recens** (B.P.C.).

*Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.). 1 in 20.

**Liquor Rhei Dulcis** (B.P.C.). *Syn.* ELIXIR RHEI.

*Dose.*—1 to 3 drachms (4 to 12 ml.).

A flavoured preparation containing 25% v/v of liquid extract of rhubarb.

**Mist. Gent. c. Rho** (N.I.F.). Sodium bicarbonate 10 gr., concentrated infusion of rhubarb 15 m., concentrated compound infusion of gentian 15 m., peppermint water to  $\frac{1}{2}$  oz.

**Mist. Rhei Ammon. c. Soda** (N.I.F.). Powdered rhubarb 4 gr., sodium bicarbonate 15 gr., ammonium carbonate 3 gr., peppermint water to  $\frac{1}{2}$  oz.

**Mist. Rhei Co.** (N.I.F.). Powdered rhubarb 3 gr., light magnesium carbonate 10 gr., powdered ginger 4 gr., sodium bicarbonate 10 gr., chloroform water to  $\frac{1}{2}$  oz.

**Mistura Rhei et Cascarae** (B.P.C.).

*Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.).

Contains rhubarb 4 gr., sodium bicarbonate 12 gr., liquid extract of cascara sagrada 20 m., with liquid extract of liquorice, syrup of ginger and oil of peppermint in chloroform water to 1 oz.

**Mistura Rhei et Sodii Bicarbonatis** (B.P.C.). *Syn.* MISTURA RHEI COMPOSITA, MISTURA RHEI ET SODÆ.

*Dose.*— $\frac{1}{2}$  to 1 ounce (10 to 30 ml.).

Similar to the preceding mixture but contains no cascara.

**Pilula Rhei Composita** (B.P.).

*Dose.*—4 to 8 grains (0.25 to 0.5 g.). Contains rhubarb 25%, aloes, myrrh, hard soap, oil of peppermint and syrup of liquid glucose.

**Pilulæ ex Franck.** *Syn.* PILDORAS DE FRANCK (F.E. VIII).

Powdered rhubarb 1 g., powdered aloes 4.5 g., powdered jalap 4.5 g. Mix with a sufficient quantity of syrup and make 100 pills. *Dose.*—1 to 3 pills.

**Pulvis Rhei Compositus** (B.P.). *Syn.* GREGORY'S POWDER.

*Dose.*—10 to 60 grains (0.6 to 4 g.).

Rhubarb 25%, with heavy and light magnesium carbonates, and ginger.

**Syrupus Rhei** (B.P.C.).

*Dose.*— $\frac{1}{2}$  to 2 drachms (2 to 8 ml.).

Liquid extract of rhubarb about 1 in 14, with oil of coriander, in syrup.

**Syrupus Rhei Aromaticus** (U.S.P. XI). *Average dose.*—2 $\frac{1}{2}$  drachms (10 ml.). Aromatic tincture of rhubarb 15, potassium carbonate 0.1, in syrup to 100.

**Tabellæ Rhei et Sodii Bicarbonatis** (B.P.C.). *Syn.* RHUBARB AND SODA TABLETS.

*Dose.*—1 or 2 tablets.

Contain rhubarb 3 gr., sodium bicarbonate 1 $\frac{1}{2}$  gr., and ginger  $\frac{1}{2}$  gr.

**Tinctura Rhei Aromatica** (U.S.P. XI). *Average dose.*—60 minims (4 ml.).

Rhubarb 20, cinnamon 4, clove 4, nutmeg 2, with glycerin, alcohol and water to produce 100.

**Tinctura Rhei Composita** (B.P.).

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Rhubarb 1 in 10 with cardamom and coriander in a glycerin and alcohol 45% menstruum.

**Sarsa** (B.P.C., U.S.P. XI, P. Helv. V, Fr. C<sup>1</sup>). *Syn.* SARSA-PARILLA.

FF\*

The dried roots and rootlets of *Smilax ornata* (Liliacæ). *U.S.P.* includes also other species of *Smilax* and *S. medica*. Was formerly used in chronic rheumatism, skin affections and syphilis, but is of doubtful therapeutic value. It is mainly used in the form of decoctions in so-called "blood purifiers."

**PSORIASIS.** Sarsaparilla has unquestionable merits, but treatment must be persistent, the average period of administration being 60 days. In 19 cases, 9 were cured and 5 improved. The remaining 5 were failures. The most rapid cure was obtained in a fortnight.—H. Ritter, *Dtsch. med. Wschr.*, 1936, 1629.

**Decoctum Sarsæ Compositum (B.P.C.).**

*Dose.*—2 to 8 ounces (60 to 240 ml.).

Sarsaparilla 1 in 8, with sassafras root, guaiacum wood, mezereon, liquorice and water.

**Decoctum Sarsæ Compositum Concentratum (B.P.C.).**

*Dose.*— $\frac{1}{2}$  to 1 ounce (8 to 30 ml.). Is eight times the strength of the preceding decoction.

**Decoctum Zittmanni Fortius.** *Dose.*—3 to 6 ounces.

Sarsaparilla (cut small) 200, water 5200, maintain at 35° to 40° for 24 hours, then add potash alum 10, calomel 8, precipitated cinnabar 2. Heat on a water-bath for three hours and add bruised anise and fennel of each 10, senna leaves (cut small) 50, liquorice root (cut small) 20. Continue heating for 15 minutes, strain and press, passing sufficient water through the marc to make up to 5000.

**Decoctum Zittmanni Mitius.** *Dose.*—3 to 6 ounces.

Sarsaparilla 100, water 5200, lemon peel, cassia bark, cardamom and liquorice of each 6. Proceed as in making the stronger decoction.

Both these preparations have been used in syphilis and wasting diseases.

**Fluidextractum Sarsaparillæ (U.S.P. XI).**

*Average dose.*—30 minims (2 ml.).

1 ml. represents 1 g. of sarsaparilla.

**Syrupus Sarsaparillæ Compositus (U.S.P. XI).**

*Average dose.*— $\frac{1}{2}$  ounce (15 ml.). Fluidextract of sarsaparilla 20%, with fluidextract of liquorice, oils of sassafras and anise, methyl salicylate, alcohol and syrup.

**Hemidesmus (B.P.C.), syn. INDIAN SARSAPARILLA**, is the dried root of *H. indicus* (Asclepiadacæ), and is used in India as a substitute for sarsaparilla.

**Taraxacum (B.P.C., P. Helv. V).** *Syn.* DANDELION ROOT.

The fresh or dried root of *Taraxacum officinale* (Compositæ). A mildly laxative bitter, and stated to have a choleric action (*i.e.*, causing an increased secretion of bile by the liver).

**Extractum Taraxaci (B.P.C.).**

*Dose.*—5 to 15 grains (0.3 to 1 g.). A soft extract from the juice of the fresh root.

**Extractum Taraxaci Liquidum (B.P.C.).**

*Dose.*— $\frac{1}{2}$  to 2 drachms (2 to 8 ml.). 1 in 1.

The following method of preparation is recommended. Moisten the drug with alcohol 30%, pack in a percolator and macerate for four days. Percolate slowly reserving the first 850 ml. Press the marc, mix the pressings with the remainder of the percolate, and evaporate the mixture to a soft extract. Dissolve the latter in the reserved portion of the percolate, adjust to volume with alcohol 30%, allow to stand for 14 days and filter.—H. D. Botwal, *Pharm. J.*, 1/1938, 461.

**Succus Taraxaci (B.P.C.).**

*Dose.*—1 to 2 drachms (4 to 8 ml.).

The juice from the fresh root preserved with alcohol.

## SACCHARINUM

*B.P.C., U.S.P. XI, P. Helv. V, P. Ned. V, Fr. Cx.*



*Syn. and Prop. Name.* GLUSIDUM, GLUSIDE, *o*-BENZOICSULPHINIDE, BENZOSULPHINIDUM, SAXIN (*Burroughs Wellcome, London*).

*Dose.*— $\frac{1}{2}$  to 2 grains (0.03 to 0.12 g.) or more. *U.S.P. XI* average dose  $\frac{1}{2}$  grain.

A white, intensely sweet, crystalline powder. Its aqueous solution has an acid reaction; it forms crystalline, sweet salts with alkaloids and metallic bases. Solutions of alkalis and their carbonates dissolve it, forming compounds.

*Soluble* 1 in 400 of water, 1 in 38 of alcohol 90%, 1 in 100 of ether, and about 1 in 50 of glycerin; slightly soluble in chloroform, oils, fats and acetone.

*Uses.* Saccharin is used as a sweetening agent and as a substitute for sugar in diabetes, obesity, and generally where the use of sugar is undesirable. It is more commonly employed in the form of soluble saccharin. As a sweetening agent to replace sugar the average proportion used is about 1 in 10,000, or about  $\frac{1}{10}$  gr. in each fluid ounce.

Saccharin (insoluble) is sold in sweetening powers 300, 450 and 550—the above remarks refer to “550.”

The most recent pharmacological, toxicological and clinical investigations have confirmed the fact that saccharin is a completely harmless substitute for sugar even when used continuously.  $1\frac{1}{2}$  to 3 grains of saccharin are sufficient to replace the whole of the sugar required by an adult for daily sweetening, i.e., 50 to 57 g. As much as 5 g. daily of saccharin has been taken for a fortnight without untoward effects.—H. Staub and R. Staehelin, *Med. Pr.*, ii/1936, 419.

**Elixir Saccharini** (*B.P.C.*). *Syn.* ELIXIR GLUSIDI.

*Dose.*—5 to 20 minims (0.3 to 1.2 ml.).

Saccharin 1 in 20 dissolved with sodium bicarbonate in alcohol and water. 1% added to mixtures for flavouring.

**Tabellæ Saccharini** (*B.P.C.*) contain  $\frac{1}{2}$  gr. (0.02 g.) of soluble saccharin.

**Saccharinum Solubile** (*B.P., U.S.P. XI, P.G. VI, P. Helv. V, P. Dan.*). *Syn.* GLUSIDUM SOLUBILE.

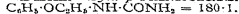


*Dose.*— $\frac{1}{2}$  to 2 grains (0.03 to 0.12 g.).

The sodium derivative of saccharin, of which it contains about 90%. Occurs as a white crystalline or granular powder.

*Soluble* 1 in  $1\frac{1}{2}$  of water at 25°, 1 in 50 of alcohol 90% at 25°. As a sweetening agent, 1 in 2000 or 2 gr. to an 8-oz. mixture is sufficient.

**Dulcin.** *Syn.* *p*-PHENETOLCARBAMIDE (*P.G. VI*).



*Dose.*—Tablets are made containing  $\frac{1}{2}$  grain (0.05 g.).

White crystalline powder, m.p. 172° to 174°. Slightly soluble in water, readily in alcohol. Used as a substitute for sugar, and stated to be innocuous.

## SANTONINUM

(with ARECA and CHENOPODIUM, etc.)

*B.P., U.S.P. XI, P. Helv. V, Fr. Cx., etc.*



**Dose.**—1 to 3 grains (0.06 to 0.2 g.). *U.S.P. XI* average dose 1 grain. *Fr. Cx.* has max. single dose  $1\frac{1}{2}$  grains, max. during 24 hours 5 grains approx. In determining the dose for a child it is a good rule to give  $\frac{1}{8}$  gr. for every year of age. Owing to the possibility of idiosyncrasy, the first dose should not exceed 1 grain for a child, or 3 grains for an adult. It is advisable not to give santonin on an empty stomach.

A neutral crystalline principle. The inner anhydride, or lactone, of santonin acid, obtained from santonica. M.p.  $171^{\circ}$  to  $174^{\circ}$ . Should be protected from light, otherwise it turns yellow (*see Golden Santonin*).

**Soluble** 1 in 50 of alcohol 90%, 1 in 3 of boiling alcohol 90%, 1 in  $2\frac{1}{2}$  of chloroform, 1 in 140 of ether, 1 in 200 of castor oil; also soluble in other oils and in caustic soda solution. Insoluble in water.

**Antidotes.** Empty stomach by emetic or stomach tube. Give purgative dose of calomel. Demulcent drinks, but *not* oils or fats. Chloral hydrate by rectum for convulsions. Stimulants. Artificial respiration if necessary.

In children, 0.06 g. has produced serious poisoning, and two such doses have been fatal.—*J. Amer. med. Ass.*, ii/1935, 1212.

**Uses.** It is an anthelmintic for round-worms (*Ascarides*) and thread-worms (*Oxyures*), but is ineffective against tape-worm (*Tænia*). It colours the urine orange if acid, or purplish red if alkaline, and in too large a dose may cause objects to appear of a green or yellow colour. The usual custom is to give the santonin in powder on 2 or 3 nights, following by castor oil or a saline purge in the morning. The flow of bile is particularly useful in making the worm let go its hold. Given in powder, the drug is not absorbed and is non-toxic. It is often given with calomel or compound powder of scammony, the subsequent administration of a purge being then unnecessary.

**Confectio Santonini Composita** (*P.E.H.C.*). Santonin 1 gr., ginger 1 gr., jalap 3 gr., sulphur 4 gr., confection of senna 51 gr. For a child 2 to 5 years.

**Tabellæ Santonini** (*B.P.C.*) contain 1 gr. (0.06 g.), in chocolate basis.

**Tabellæ Santonini et Hydrargyri Subchloridi** (*B.P.C.*).  
*Syn.* TABELLÆ SANTONINI COMPOSITÆ.

**Dose.**—1 or 2 tablets.

Contain santonin 1 gr. and mercurous chloride 1 gr.

**Tabellæ Santonini et Scammonia Compositæ** (*B.P.C.*).

**Dose.**—1 tablet.

Contain santonin  $1\frac{1}{2}$  gr., compound powder of scammony 2 gr.,



and mercurous chloride  $\frac{1}{2}$  gr. **Pulvis Santonini Compositus** (*Gt. Orm. H.*) has the same composition. A saline should be given next morning.

**Trochisci Santonini** (*B.P.C.*) contain 1 gr.

**Golden Santonia.** *Syn.* CHROMO-SANTONIN.

*Dose.*—2 to 5 grains (0.12 to 0.3 g.).

A modification of ordinary santonin formed by exposure to sunlight, and stated to be of value in sprue and dysentery.

**Sodii Santoninas.**  $\text{NaC}_{15}\text{H}_{19}\text{O}_4 \cdot 3\frac{1}{2}\text{H}_2\text{O} = 349.2$ .

*Dose.*— $\frac{1}{4}$  to 1 grain (0.016 to 0.06 g.) for adults. White crystals. Should in preference be given in salol-coated pills or tablets. Has been used as anthelmintic.

**Santonica** (*B.P.C.*). *Syn.* SEMEN CONTRA (*P. Helv. V*), SEMEN CINÆ, WORMSEED, FLORES CINÆ (*P.G. VI, P. Dqn.*).

The dried unexpanded flower heads of *Artemisia cina* (*Compositæ*). Contains 2 to 3.5% of santonin. Has been administered as a decoction or infusion for round-worms and thread-worms. *Fr. Cx.* includes *A. maritima*.

Santonin from Scottish-grown *Artemisia maritima*; 0.81% found.—J. Coutts, *Pharm. J.*, ii/1929, 603.

The examination of true and false santonicas.—T. E. Wallis and E. J. Mowat, *Pharm. J.*, ii/1925, 149.

Two new crystalline principles isolated from Indian species of *Artemisia*.—*Pharm. J.*, i/1935, 3.

**Absinthium** (*B.P.C., P. Helv. V, Fr. Cx.*). *Syn.* WORMWOOD.

The dried leaves and tops of *Artemisia Absinthium* (*Compositæ*). The active ingredient is the oil (0.3%). It is used as a tonic and digestive. Infusion 1 in 20.

*Dose.*—1 to 2 ounces. The oil is contained in the drink absinthe. Other essential oils, e.g., anise, coriander, fennel, peppermint, hyssop, angelica and melissa are stated to be additional constituents.

**Tinctura Absinthii** (*B.P.C.*).

*Dose.*—1 to 4 drachms (4 to 16 ml.). 1 in 10.

**Areca** (*B.P.C., Fr. Cx.*). *Syn.* SEMEN ARECÆ (*P.G. VI, P. Helv. V*), BETEL NUT.

*Dose.*— $\frac{1}{4}$  to 1 drachm (1 to 4 g.).

The dried ripe seeds of *Areca Catechu* (*Palmaceæ*). Contains several alkaloids, the most active being the liquid alkaloid arecoline (about 0.1%),  $\text{C}_8\text{H}_{13}\text{NO}_2 = 155.1$ .

**Uses.** Areca nut has been used for a long time in India and China as an anthelmintic, but recent work has thrown considerable doubt on its value. While it has undoubtedly an irritant action on the gut and produces purgation, it does not expel worms. As a vermifuge for tape-worm in dogs it is given in doses of 2 gr. per lb. bodyweight. The nut is also widely used in the East as a masticatory, owing to its sialogogue properties.

**Arecolinæ Hydrobromidum** (*P.G. VI, Fr. Cx., etc.*).

$\text{C}_8\text{H}_{13}\text{O}_2\text{N} \cdot \text{HBr} = 236.0$ .

*Dose.*—*P. Helv. V* gives max. single dose  $\frac{1}{32}$  gr., max. in 24 hours  $\frac{1}{10}$  grain approx.; *Fr. Cx.* has  $\frac{1}{16}$  and  $\frac{1}{8}$  grain respectively.

White needles soluble in water and boiling alcohol.

Its physiological action resembles that of physostigmine and pilocarpine. It is sialagogue and diaphoretic and causes constriction of the pupil and slowing of the heart. A 1% solution has been used as a miotic but action is of short duration. It is given hypodermically as a cathartic in veterinary medicine, the dose for horses

being about 1 grain; also given orally in doses of  $\frac{1}{16}$  to  $\frac{1}{2}$  grain as a tænicide for dogs after a preliminary period of fasting.

**Buteæ Semen (B.P.C.).**

*Dose.*—10 to 20 grains (0.6 to 1.2 g.).

The seeds of *Butea frondosa* (Leguminosæ). Contains moodooga oil. Anthelmintic like santonin. Administered as **Pulvis Buteæ Seminum**, the integuments being removed by soaking in water, the seeds then being dried and powdered.

**Chenopodium (B.P.C.). Syn. AMERICAN WORMSEED.**

*Dose.*— $\frac{1}{4}$  to 1 drachm (1 to 4 g.).

The fruit of *C. ambrosioides* var. *anthelminticum* (Chenopodiaceæ). Contains 1% of volatile oil containing about 70% of ascaridole. Is a vermifuge for round-worms and hook-worms, but the volatile oil is now generally preferred.

**Oleum Chenopodii (B.P., U.S.P. XI, P. Helv. V). Syn. OIL OF AMERICAN WORMSEED.**

*Dose.*—3 to 15 minims (0.2 to 1 ml.). *U.S.P. XI* average dose 15 minims. *P. Ned.* has max. daily dose 22 minims.

The oil distilled with steam from the fresh flowering and fruiting plants of *Chenopodium ambrosioides* var. *anthelminticum*. Contains not less than 65% *w/w* of ascaridole,  $C_{10}H_{16}O_2$ . *U.S.P. XI* requires 60 to 80% of an acetic acid soluble fraction.

**Antidotes.** A purgative should be given, followed by an enema; alcohol should be withheld and warmth applied to the body. Respiratory and cardiac stimulants should be given.

**Uses.** Oil of chenopodium is an effective anthelmintic, especially against round-worms and hook-worms, but it has little or no action on large tape-worms. The drug does not kill the worms but only paralyzes them, and they must be expelled by a purgative. For the treatment of hook-worms the drug is best given in the morning, in doses of 10 to 15 m. in capsules or on sugar, at 7, 8, and 9 a.m.; some authorities prefer to give two doses of 20 m. with an interval of two hours between the doses. The last dose should be followed within two or three hours by a purgative dose of castor oil or magnesium sulphate. For children, one drop of oil of chenopodium for each year of age is given on sugar. A more effective treatment for hook-worms consists in the administration of a mixture of 1 volume of oil of chenopodium with 2 volumes of carbon tetrachloride, and this is given in a dose of  $1\frac{1}{2}$  m. for each year of age up to a maximum of 25 m.; the total amount is divided into two doses, given one hour apart and followed by a purgative. The treatment requires weekly repetition until the fæces are free from ova.

For the treatment of round-worms in children a dose of 5 to 10 m. on sugar is given two or three times daily for two days, followed by a purge. The treatment should be repeated after ten days or a fortnight.

Oil of chenopodium should be given with caution and in small doses when disorders of the heart and kidneys are present. It is contraindicated in chronic nephritis and organic disease of the heart, and in the presence of hepatic or gastro-intestinal disorder.

Even with therapeutic doses, minor toxic effects such as dizziness, nausea, tinnitus, and temporary deafness, frequently occur, and cumulative effects may be produced by small doses given several days apart. Children are more susceptible to the effects of the oil than adults, and it is better to use some other anthelmintic in children under 5 or 6 years of age, and in very old and debilitated subjects.

Oil of chenopodium has no stability. When in greatest vogue its active principle, ascaridole, was still undetermined. This is deadly to man and worm, the respective lethal doses lie near one another, and its reported percentage in the oil has varied from 33 to 98. Further, the size of drops varies with different droppers, and there has been catastrophic confusion between 45 drops on the International Dropper (or 2.2 ml.) and 45 minims (or 3 ml.). Numerous deaths have followed the latter, apparently none the former, which at a percentage of 66 implies 0.8 ml. of ascaridole. To give the oil without knowledge of its ascaridole content is indefensible—but customary. Many tens of thousands of doses have been reported, in few has its ascaridole content been known, and in none of these has deworming been the method of measurement. In other words, I find no acceptable published evidence of its efficiency against hookworms.—C. Lane, *Lancet*, i/1935, 1461.

**Ascaridole.**  $C_{10}H_{16}O_2 = 168.23$ . The separated active principle of oil of chenopodium. *Dose*.—Adults, 12 to 20 minims (max. 30 minims). To be given in three portions at intervals of 1 hour. Children  $\frac{1}{4}$  to  $\frac{1}{2}$  minims for a child of 2 years, increasing by  $\frac{1}{2}$  minim for every year of age up to 12, then by 1 minim per year up to adult age. May be administered on sugar or in any suitable vehicle. Castor oil or magnesium sulphate should be given after the last dose.

**Bedermin** (*Bayer Products, London*). A combination of ascaridole and carbon tetrachloride in the proportion of 1 to 6. An anthelmintic for use against ankyllostoma and ascariis. Supplied in solution and capsules.

**Cucurbita** (*B.P.C., P. Helv. V*). *Syn.* CUCURBITÆ SEMINA PRÆPARATA, MELON PUMPKIN SEEDS, PEPO.

*Dose*.—3 to 4 ounces, bruised, with water or milk to one pint. The fresh ripe seeds of *C. maxima* (Cucurbitaceæ), deprived of testa and tegmen, and not more than a month old. Anthelmintic; give first a saline purge and afterwards castor oil.

Although no active principles have been found, it is of undoubted value as a tænicide, the therapeutic activity being probably due to the mechanical action of the sharp edges of the bruised seeds.

**Cusso** (*B.P.C.*). *Syn.* KOUSSO.

*Dose*.— $\frac{1}{2}$  to 1 ounce (8 to 16 g.) made into an infusion.

The dried panicles of fertilised pistillate flowers of *Brayera anthelmintica* (Rosaceæ). Contains the yellow amorphous body, kosotoxin. Anthelmintic, especially for tape-worm. Administered as an infusion (1 in 16), the dose being preceded by the administration thrice daily of 1 drachm doses of sodium bicarbonate, and by a saline purge, being taken on an empty stomach. Its use is contraindicated in pregnancy, debility, and in cardiac and renal disease.

**Embelia** (*B.P.C.*).

*Dose*.—1 to 4 drachms (4 to 16 g.). Dried fruit of *E. ribes* and *E. robusta* (Myrsinaceæ). Has been advocated as an anthelmintic for hook-worms, round-worms and tape-worms, but is of doubtful value.

## SAPONES

**Sapo Animalis** (*B.P., Fr. Cx.*). *Syn.* CURD SOAP.

Curd soap is made by heating purified animal fat with water. It consists mainly of sodium stearate.

Sparingly *soluble* in cold water, completely soluble in hot water, almost completely soluble in alcohol 90%.

[P1-S1-S3] **Emplastrum Saponis Fuscum** (B.P.C.). *Syn.* EMPLASTRUM CERATI SAPONIS. Curd soap, yellow beeswax, olive oil, lead monoxide and vinegar. The machine-made plaster is usually spread with three to four ounces of mass per yard of bleached glazed calico.

**Linimentum Saponis Camphoratum** (B.P.C.). *Syn.* SOLID OPODELDOC. A solid liniment containing curd soap, camphor, oils of thyme and rosemary, dilute solution of ammonia and alcohol.

**Sapo Durus** (B.P. *Add. III*, U.S.P. *XI Supp. II*). *Syn.* CASTILE SOAP.

Hard soap is prepared by saponifying a suitable vegetable oil or oils, or their fatty acids, with sodium hydroxide. Coconut oil or palm kernel oil, or their fatty acids, must not be used.

**Soluble** in water and alcohol.

[P1-S1-S3] **Emplastrum Saponis** (B.P.C.). Hard soap, colophony and plaster of lead. Is less adhesive than plaster of colophony. The machine spread plaster is usually prepared with not less than  $3\frac{1}{2}$  oz. of mass per yard of bleached glazed calico.

[D-P1-S1] **Pilulæ Saponis cum Opio** (B.P.C.). *Syn.* PILULÆ SAPONIS COMPOSITÆ, COMPOUND SOAP PILLS.

Each pill contains  $\frac{3}{8}$  gr. of powdered opium and about 1 gr. of hard soap. *Dose.*—1 or 2 pills.

**Sapo Kalinus** (B.P.C., P.G. *VI*, P. *Helv. V*). *Syn.* LINSEED OIL SOAP.

Potash soap is made by heating linseed oil with potassium hydroxide.

**Soluble** about 1 in 4 of water, 1 in 1 of alcohol 90%.

**Sapo Amygdalinus** (F.E. *VIII*). *Syn.* SAPO MEDICINALIS (Fr. *Cx.*). Made from almond oil and sodium hydroxide. **Sapo Medicatus** (P.G. *VI*, P. *Dan.*, P. *Helv. V*) is made from lard and olive oil.

**Spiritus Saponis Kalini** (B.P.C.). *Syn.* SPIRITUS SAPONIS KALINI (HEBRA). An alcoholic solution of potash soap, perfumed with oil of lavender.

**Liquid Soap Formula.** Oleic acid 35, S.V.R. 25, potassium hydroxide 7, distilled water 7, oil of lavender 0.2, light petroleum to 100. Mix the oleic acid with the alcohol, slowly add a solution of the potassium hydroxide in the water, then the oil of lavender and part of the solvent. Adjust the pH until neutral to phenolphthalein with oleic acid and make up to volume with light petroleum.—H. Finnemore, *Aust. J. Pharm.*, 1938, 19.

**Sapo Mollis** (B.P. *Add. III*). *Syn.* SAPO VIRIDIS.

Soft soap is prepared by saponifying a suitable vegetable oil or oils, or their fatty acids, with potassium or sodium hydroxide. Coconut oil or palm kernel oil, or their fatty acids, must not be used. It contains the glycerin formed during saponification.

**Soluble** in water and alcohol.

**Sapo Mollis** (U.S.P. *XI*). Made from linseed oil and a mixture of potassium and sodium hydroxides, with additional glycerin.

**Enema Saponis** (B.P.C.). *Dose.*—20 ounces (600 ml.). 5% w/v.

**Linimentum Saponis** (B.P.). Soft soap 4, camphor 2, oil of rosemary 0.75, distilled water 8.5, alcohol 90% to 50.

**Linimentum Saponis Mollis** (U.S.P. *XI*). 65% of soft soap and 2% of oil of lavender in alcohol.

**Liquor Saponis Æthereus** (B.P.C.). *Syn.* ETHER SOAP, SOLUTIO SAPONIS ÆTHEREÆ.

A solution containing about 40 to 50% of potassium oleate in alcohol and ether.

[P1] **Liquor Saponis Antisepticus** (B.P.C.) is the same solution with the addition of 0.05% w/v of mercuric iodide and potassium iodide.

**Spiritus Saponatus (B.P.C.).** 65% w/v of soft soap in alcohol.

**Synol Soap (Johnson & Johnson, Slough).** A liquid soap containing 2½% of cresol.

**Sodii Oleas.** *Prop. Name.* EUNATROL (Zimmer, Frankfurt; Coates & Cooper, London).

$\text{CH}_3(\text{CH}_2)_7\text{CH} : \text{CH}(\text{CH}_2)_7\text{COONa} = 304.3.$

*Dose.*—2 to 10 grains (0.12 to 0.6 g.).

It has been used as a cholagogue and to dissolve gall-stones. Carcinoma has been treated with sodium oleate on the theory (Shaw-Mackenzie) that sodium oleate and various tissue extracts act as co-enzymes; 20 gr. of sodium oleate daily are given, in pill form for a year and 30 injections of 10 ml. of sodium oleate solution—beginning with ½% and increasing to 5%. Subcutaneous injections of 1 to 3 ml. of a 0.8% solution are said to have been found of benefit in cancer of the breast.

**Sodii Stearas (U.S.P. XI)** is a mixture of the stearate ( $\text{NaC}_{17}\text{H}_{35}\text{O}_2$ ) and palmitate ( $\text{NaC}_{15}\text{H}_{31}\text{O}_2$ ). A white powder soapy to the touch. Slowly soluble in cold water or alcohol, readily in hot. Sodium stearate cream (*Fr. Cx.*) consists of freshly prepared sodium stearate in glycerin and water.

**Saponinum (B.P.C.).** *Syn.* QUILLAIC ACID, QUILLAIN.

A colloidal glycoside or mixture of glycosides obtained from quillaia bark. An intensely irritating and sternutatory powder. Aqueous solutions froth readily when shaken. Has hæmolytic action on blood. Is used as an emulsifying agent for oils in external applications and as a foam stabiliser in contraceptive tablets.

Saponins, various, described.—J. G. Driver and A. G. Trease, *Pharm. J.*, i/1927, 623.

Usual views as to hæmolytic action of saponins when taken orally are contradicted. A man can take as a single daily dose as much as 4 g. without any damage resulting, since it does not pass through the intestinal walls and is decomposed by digestive enzymes.—L. Kofler, *Apothekerztg.*, 1933, 702.

**Sulphonated Fatty Alcohols.** The so-called "sulphonated fatty alcohols," as supplied in commerce, consist of the sodium salts of the sulphuric acid esters of the fatty or higher aliphatic monohydric alcohols. In other words they are sodium alkyl sulphates, and a more correct description would be sulphated fatty alcohols. They are prepared by the action of sulphuric or chlorosulphonic acid on the higher alcohols under carefully controlled conditions, with subsequent neutralisation with a sodium salt. As the higher alcohols, with the exception of cetyl alcohol, do not occur naturally either in the free or combined condition, they are obtained by the catalytic hydrogenation of the higher fatty acids. The chief sources of the latter are fixed oils and fats which, on hydrolysis, give mixtures of these acids which are never separated in commerce but are submitted directly to hydrogenation. Hence, the higher aliphatic alcohols consist of mixtures, the composition of which depends upon the source of the fixed oil or fat used to obtain the acid. The commonest alcohols used are "lauryl alcohol," obtained from coconut oil and consisting mainly of lauryl alcohol,  $\text{C}_{12}\text{H}_{25}\text{OH}$ , mixed with homologues with smaller and larger numbers of carbon atoms; "stearyl alcohol," a mixture

of stearyl alcohol,  $C_{18}H_{37}OH$ , and cetyl alcohol,  $C_{16}H_{33}OH$ , obtained from commercial stearic acid; "oleyl alcohol," obtained by the hydrogenation of olein; and cetyl alcohol, obtained directly from natural sources, such as spermaceti. Other synthetic compounds are available, containing sulphonic groups, more complex in structure than the foregoing. These include Igepon "A," the sulphonated ethyl ester of oleic acid, and Igepon "T," a sulphonated amide of oleic acid.

**Properties.** The use of sulphonated fatty alcohols overcomes many of the difficulties encountered in the use of soaps. They are all white powders, soluble in water, with wetting-out, cleansing and detergent properties superior to those of soap, and they maintain their detergent powers in neutral, slightly acid or alkaline solution. The solubility of their calcium and magnesium salts is sufficiently great to avoid the formation of an objectionable precipitate when used with hard water, this property rendering them eminently suitable for use in cleansing materials before dyeing. Although they have not the smooth lubricating "feel" of soap suds they possess the softening properties of soap to a marked degree. The sulphonated fatty alcohols show a gradual alteration in properties as the number of carbon atoms in the molecule is increased. The lower members derived from alcohols possessing round about twelve carbon atoms, have the best wetting-out and penetrating properties, whereas the higher members have better detergent powers. The lower members, however, are less likely to precipitate with calcium salts. The sulphonated fatty alcohol made from oleyl alcohol, an unsaturated alcohol, has special properties, being both a good detergent and a good wetting-out agent.

**Uses.** Sulphonated fatty alcohols find extensive use in many and varied industries. Pharmaceutical applications are increasing rapidly, and include the preparation of soapless shampoo powders, toilet preparations, tooth pastes and powders. Included in cosmetics they greatly assist the removal of make-up or dirt. In the dyeing industry sulphonated fatty alcohols are used as cleansers before dyeing and they are also added to the dye-bath itself to ensure even penetration. Their powers of increasing penetration are also put to good use in the leather industry to assist the wetting of leather by water or the penetration of wet leather by oil. Sulphonated fatty alcohols are used in varnishes and paints to increase the spreading power, in adhesives to increase adhesion, and for many other purposes.

The preparation, properties and uses of sulphonated alcohols are described, and formulæ are suggested for a soapless shampoo powder, a shampoo powder containing soap and a sulphonated alcohol, and a foam bath.—N. Evers, *Pharm. J.*, i/1938, 326.

**Sulphonated Lorol** (Ronsheim & Moore, London) consists of the sodium salt of sulphated lauryl alcohol,  $C_{12}H_{25}O\cdot SO_2\cdot ONa$ , containing smaller proportions of sulphated analogous acids. Several grades of the material are available, including liquid, paste and powder. **Sulphonated Lorol L.Z.** is a special grade for use in soapless and/or acid dentifrices.

**Anti-misting Compound.** Sodium oleyl sulphate 18%, titanium dioxide 27%, alcohol 33%, water 22%, all by weight. The preparation is made by grinding the ingredients together to form a liquid of uniform consistence. A surface treated by spreading the material evenly with a soft cloth should dry and be capable of being lightly polished by a soft dry cloth in three minutes.—Air Ministry Specification (D.T.D. 338, H.M.S.O.), per *Pharm. J.*, i/1940, 105.

**Sodii Sulphoricinas.** *Syn.* TURKEY RED OIL, ALIZARINE OIL.

Sodium sulphoricinate is the sodium salt of sulphonated castor oil, obtained by adding sulphuric acid to castor oil, and treating the product with sodium hydroxide. It is a yellow or yellowish red viscous liquid, with a faint odour, giving a clear solution when diluted with an equal volume of water, and a stable emulsion with nine times its volume of water.

**Uses.** Sodium sulphoricinate and other true sulphonated oils have not found a very extensive use in pharmacy. They are not as effective detergents as the sulphonated fatty alcohols, but they are sometimes used in soapless shampoos and permanent waving lotions to increase the wetting power. Sodium sulphoricinate is used as a constituent of perfume sprays, in hand cleansers, motor soaps, etc. It finds its most extensive use in the dyeing industry as a fixing agent and as an emulsifying agent. It was particularly used for the treatment of cotton to be dyed with turkey red or alizarine. A concentrated solution of sodium sulphoricinate will dissolve iodine, resorcinol and naphthalene, forming antiseptic solutions. It has been used as a glycerin substitute.

The following formulæ for ointment bases have been found useful: (a) Lanette wax S.X. 10, avocado pear oil 10, turkey red oil 10, lanolin 10, water 30, benzoinated lard 30. This is all but completely absorbed. (b) Turkey red oil 5, water 10, Eucerin 85, which leaves a greasy surface, and (c) coconut oil soap 10, hydrous wool fat 10, coconut oil 20, turkey red oil 10, P.M.B. 333 5, stearyl alcohol 5, white soft paraffin 40.—Bamber, *Brit. J. Derm. & Syph.*, 1940, 52, 21.

[P2] **Phenol Sodio-Sulphoricinate.** A mixture of phenol 1, and sodium sulphoricinate 4. A thick syrup miscible with water. 20 to 50% solution has been used for papilloma and tuberculosis of larynx and for ozæna.

Pharyngo-keratosis (mycosis) has been treated with 10% solution, also 10% solution of salicylic acid in the sulphoricinate.

**Triethanolamina (B.P.C.).** *Syn.* TRIETHYLOLAMINE.

A colourless, almost odourless, syrupy liquid with strongly alkaline reaction, which darkens on exposure to air. Consists chiefly of trihydroxytriethylamine,  $(\text{CH}_2\text{CH}_2\text{OH})_3\text{N}$ , with small proportions of the di- and monohydroxy compounds. Forms crystalline salts with mineral acids; the hydrochloride has m.p.  $173^\circ$  to  $174^\circ$ .

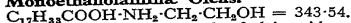
**Miscible** with water and alcohol 90%; soluble in chloroform; less soluble in benzene and ether.

Is a useful emulsifying agent for preparations for external use when used in conjunction with oleic or stearic acid, with which the corresponding salts are formed. Also used as a solvent for casein, shellac and dyes.

**Triethanolaminæ Stearas.** The triethanolamine salt of stearic acid. A yellowish-brown solid, soluble in water. Used as an emulsifying agent instead of ordinary soaps for oils and fats.

Useful in toilet preparations to avoid alkalinity of sodium and potassium soaps, and in the manufacture of creams and polishes.

### Monoethanolaminæ Oleas.



The monoethanolamine salt of oleic acid, occurring as a colourless, deliquescent solid. It is used as a 5% solution containing 25% of glycerin or 2% of benzyl alcohol for the injection treatment of varicose veins in doses of 1 to 2 ml. at each site, with a maximum of 6 ml. altogether on one occasion. The doses should be repeated at weekly intervals.

Monoethanolamine oleate is the most satisfactory of the sclerosing agents. Morrhuate and quinine urethane solutions have their contraindications, while salicylates tend to be painful. None of these disadvantages attends the use of the oleate solution, and as it is only slightly irritant to the perivenous tissues, ulceration is not likely to occur if a little escapes through the puncture into the vein.—L. Rogers, *Brit. med. J.*, ii/1939, 385.

**Ethamolin** (*Glaxo Laboratories, London*). Aqueous solution of ethanolamine oleate 5%, with benzyl alcohol 2%, supplied in 2 ml. ampoules and 15 and 30 ml. bottles for the injection treatment of varicose veins.

**E.O.B.A. Sclerosant** (*Wyleys, Coventry*). A 5% solution of monoethanolamine oleate with benzyl alcohol 2%, supplied in 15 ml. and 50 ml. rubber-capped bottles and in 2 ml. ampoules.

**Monolate** (*Abbott Laboratories, London*). Monoethanolamine oleate 5%, in ampoules. For injection treatment of varicose veins.

**Moramin** (*Allen & Hanburys, London*). A 5% preparation of ethanolamine morrhuate, for the injection treatment of varicose veins, issued in 20 ml. vials. Dose.—1 to 2 ml. at each site, with a max. of 6 ml. on any one occasion.

### Triisopropanolamina. $N(C_3H_7OH)_3 = 159.27$ .

A colourless, pasty, semicrystalline mass with a slight odour and a bitter taste; m.p.  $46^\circ$ .

Readily **soluble** in water, alcohol, acetone, ether and chloroform. It is used in the preparation of Sobisminol Mass (*q.v.*).

A mixture of di-, tri- and mono-isopropanolamines containing about 43% each of the di- and tri-, and about 10% of the mono- substance, possessed greater emulsifying powers for pharmaceutical and cosmetic preparations than tri-isopropanolamine alone. In addition, salts of this mixture were softer and lighter than the salts of either tri- or mono-isopropanolamine.—G. W. Fiero, *J. Amer. pharm. Ass.*, 1939, 1036.

**Quillaia** (*B.P., P. Helv. V, Fr. Cx.*). *Syn.* PANAMA BARK, SOAP BARK.

*Dose.*—1 to 3 grains (0.06 to 0.2 g.).

The dried inner part of the bark of *Quillaia Saponaria* and other species (*Rosaceæ*). Contains quillaic acid,  $C_{19}H_{30}O_{10} = 418.3$ , and sapotoxin,  $C_{17}H_{28}O_{10} = 408.2$ , closely allied to saponin. Has a sweetish but acrid after-taste and possesses emulsifying properties, causing frothing in water in which it has been macerated. Its lather kills pediculi of scalp. Soap bark has been used as an expectorant in bronchitis; is contraindicated in inflammation of the intestines or stomach, or ulcerated condition of the mucous membrane. The powdered bark is a powerful sternutatory.

**Extractum Quillaie Liquidum** (*B.P.C.*). 1 in 1.

**Tinctura Quillaie** (*B.P.*).

1 in 20 of alcohol 45%. Five minims of this will emulsify 1 drachm of fixed oil.



## SCILLA

*B.P., U.S.P. XI, P. Helv. V, Fr. Cx., etc.*

*Syn. SCILLÆ BULBUS (I.A.), WHITE SQUILL.*

*Dose.*—1 to 3 grains (0.06 to 0.2 g.). *Fr. Cx.* has max. single dose  $7\frac{1}{2}$  grains; max. in 24 hours 15 grains.

The bulb of *Urginea Scilla* (Liliaceæ) (*U. maritima* *U.S.P. XI*) with membranous outer scales removed, cut into slices and dried.

*As a war emergency measure, when Squill is prescribed, or demanded, Indian Squill may be dispensed or prescribed.*

**Antidotes.** Treat as for poisoning by digitalis, see p. 480.

**Uses.** Squill closely resembles digitalis in its action, but is a more powerful gastro-intestinal irritant and a more energetic diuretic. Because of its irritant properties it is seldom given alone, but is frequently combined with digitalis in the treatment of heart disease or as a diuretic. A favourite diuretic pill is composed of 1 gr. each of powdered digitalis, squill, and pill of mercury. Squill also has an expectorant action. It is too irritating to the bronchial mucous membrane for use in acute bronchitis, but is of value in chronic bronchitis when the secretion is scanty. The use of squill is contraindicated in Bright's disease.

The powdered drug, and extracts made from it, have been largely used as rat poisons and are said to be very efficacious; the red variety is usually preferred for this purpose.

**Red Squill.** Red squill has a similar content of cardiac glycosides to white squill, as shown by Wokes and Willimott (*Quart. J. Pharm.*, 1934, 565). It has in addition constituents which are toxic for rats, and is therefore used as a rat poison. These are not wholly absent from white squill. Wokes and Willimott (*loc. cit.*) found that when they prepared a dried powder from the two varieties, the dose of the red squill necessary to kill half the rats was 1.0 to 1.5 g. per kg., whereas the dose of the white squill was ten times as great. These doses were given by mouth.

The rat-poisoning substances appear to be present in significant amounts in the red squills only.—F. R. Winton, *J. Pharmacol.*, June, 1927, 137.

Liquid extract of red squill is efficacious. Add to bread and milk. Comparatively harmless to larger animals, advocated by Min. of Agriculture.—*Pharm. J.*, ii/1927, 524.

**Acetum Scillæ (B.P., U.S.P. XI).**

*Dose.*—10 to 30 minims (0.6 to 2 ml.).

Squill 10% w/v macerated in dilute acetic acid.

**Extractum Scillæ Liquidum (B.P.C.).**

*Dose.*—1 to 3 minims (0.06 to 0.2 ml.). 1 in 1.

**Extractum Scillæ (Fr. Cx.).** *Max. single dose.*—0.2 g. A soft extract prepared with alcohol 60%.

**Linctus Scillæ (B.P.C.).** *Syn. LINCTUS, SIMPLE LINCTUS.*

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Oxymel of squill 1 in 4 with mucilage of tragacanth, glycerin, emulsion of chloroform and syrup.

**Linct. Simplex (N.I.F.).** *Dose.*—1 drachm (4 ml.).

Oxymel of squill, syrup of tolu and glycerin, equal parts.

[P1] **Mist. Expect. Nig. (N.I.F.).** Ammonium carbonate  $3\frac{1}{2}$  gr., liquid extract of squill 2 m., camphorated tincture of opium 15 m., syrup of tolu 15 m., solution of burnt sugar  $7\frac{1}{2}$  m., chloroform water to  $\frac{1}{2}$  oz.

**Oxymel Scillæ (B.P.).**

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Contains equivalent of 5% *w/v* of squill in acetic acid, honey, and distilled water.

**Mist. Oxymellis (N.I.F.).** Oxymel of squill 30 m., liquid extract of ipecacuanha  $\frac{1}{2}$  m., glycerin 20 m., dilute sulphuric acid 4 m., solution of bordeaux B 2 $\frac{1}{2}$  m., water to  $\frac{1}{2}$  oz.

[P1] **Mist. Scillæ Co. (N.I.F.).** Oxymel of squill 30 m., camphorated tincture of opium 15 m., liquid extract of ipecacuanha  $\frac{1}{2}$  m., water to  $\frac{1}{2}$  oz.

**Pillule Scillæ Compositæ (B.P.C.).**

*Dose.*—1 or 2 pills.

Contain squill 1 gr., ginger  $\frac{1}{2}$  gr., ammoniacum  $\frac{1}{2}$  gr., and hard soap about  $\frac{1}{2}$  gr.

**Syrupus Scillæ (B.P.).**

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Contains 45% *v/v* of vinegar of squill.

**Syrupus Scillæ (U.S.P. XI).** *Average dose.*—30 minims (2 ml.).

Vinegar of squill 45, sucrose 80 in water to 100.

**Tinctura Scillæ (B.P.).**

*Dose.*—5 to 30 minims (0.3 to 2 ml.).

Contains equivalent of 10% *w/v* of squill.

**Tinctura Scillæ (U.S.P. XI).** *Average dose.*—15 minims (1 ml.).

Strength 1 in 10.

**Scillaren (Sandoz, London; Brooks & Warburton, London).** Preparations of the total glycosides of squill. *Dose.*—2 tablets (ea. 0.0008 g.) or 40 drops of solution (0.0008 g. per ml.) 3 or 4 times daily; in urgent cases intravenously not more than 1 ampoule (1 ml. = 0.0005 g.) per day. Valvular lesions, œdema of cardiac origin, chronic myocarditis and "weak heart."

**Urginea (B.P.C.). Syn. INDIAN SQUILL.**

*Dose.*—1 to 3 grains (0.06 to 0.2 g.).

The bulb of *U. indica* with membranous outer scales removed, cut into slices and dried.

**Uses.** As for squill. As a war emergency measure (1941) it may be dispensed or supplied when squill is prescribed or demanded.

**SENEGA**

*B.P., P. Helv. V, Fr. Cx.*

*Dose.*—6 to 12 grains (0.4 to 0.8 g.).

The dried root of *Polygala Senega* (Polygalaceæ) containing glycosidal saponins, senegin and polygalic acid, and a fixed oil.

Senega is a reflex expectorant and is employed, usually with other expectorants, such as ipecacuanha and squill, in bronchitis.

**Polygalitol**, an anhydride of mannitol and isomeric with styracitol has now been isolated from the fresh flowering plants and also from the dried roots of *Polygala Senega* as a white crystalline powder. It has a sweet taste, but does not reduce Fehlings solution.—C. J. Carr and J. C. Krantz, *J. Amer. pharm. Ass.*, 1938, 21, 318.

**Extractum Senegæ Liquidum (B.P.).**

*Dose.*—5 to 15 minims (0.3 to 1 ml.).

1 in 1 of alcohol 60%, rendered faintly alkaline with ammonia.

**Infusum Senegæ Concentratum (B.P.).**

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 3 ml.).

1 in  $2\frac{1}{2}$  of alcohol 25%, rendered faintly alkaline with ammonia.

**Infusum Senegæ Recens (B.P.).**

*Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.). 1 in 20.

**Tisane de Polygala (Fr. Cx.).** 1 in 100 of boiling water; infuse  $\frac{1}{2}$  hour.

**Mist. Seneg. Ammon. (N.I.F.).** *Syn.* MIST. IPECAC. CO.

Ammonium carbonate 3 gr., tincture of ipecacuanha 5 m., liquid extract of squill 2 m., liquid extract of senega 6 m., water to  $\frac{1}{2}$  oz.

**Tinctura Senegæ (B.P.).**

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Liquid extract of senega 1 in 5, with alcohol 60%.

**Cocillana. *Syn.* GUAPI BARK.**

*Dose.*—8 to 15 grains (0.5 to 1 g.).

The bark of a South American plant, *Guarea Rusbyi* (Meliaceæ), stated to equal ipecacuanha in expectorant properties and to be, in addition, tonic and laxative.

**[P1] Syrup. Cocillanæ Co. (D.T.F.).**

Liquid extract of cocillana (1 in 1, with alcohol 60%) 16 m., liquid extract of euphorbia 40 m., liquid extract of squill 4 m., liquid extract of senega 4 m., potassium antimonytartrate  $\frac{1}{2}$  gr., codeine phosphate 2 gr., water 60 m., menthol  $\frac{1}{2}$  gr., spirit of chloroform 40 m., glycerin 160 m., syrup to 2 oz.

**[P1] Cosylan (Syrup Cocillana Compound) (Parke, Davis, London).** Expecto-  
rant combination, containing per oz.: tincture of cocillana 40 m., tincture of  
euphorbia 120 m., syrup of wild lettuce 120 m., fluid extract of squill 2 m.,  
fluid extract of senega 2 m., potassium antimonytartrate  $\frac{1}{2}$  gr., cascarn 8 gr.,  
ethylmorphine hydrochloride  $\frac{3}{4}$  gr., menthol  $\frac{1}{8}$  gr. *Dose.*— $\frac{1}{2}$  to 1 drachm  
3 or 4 times daily.

**Prunus Serotina (B.P., U.S.P. XI). *Syn.* PRUNI VIRGINIANÆ  
CORTEX, WILD CHERRY BARK.**

*Dose.*—15 to 30 grains (1 to 2 g.).

The bark of *Prunus serotina* (Rosaceæ). Contains prunasin and  
a cyanogenetic enzyme, and may yield from 0.075 to 0.16% of  
HCN. Used for relief of cough in phthisis, bronchitis, etc.

**[P1] Syrupus Pruni Serotinæ (B.P.). *Syn.* SYRUPUS PRUNI VIR-  
GINIANÆ, SYRUP OF WILD CHERRY.**

*Dose.*— $\frac{1}{2}$  to 2 drachms (2 to 8 ml.).

A solution of sucrose in an aqueous glycerin percolate, con-  
taining the equivalent of 15% w/v of the bark. It is reported that  
a preparation made by percolation with water only is lighter,  
contains less tannin and has less tendency to deposit.

**[P1] Syrupus Pruni Virginianæ (U.S.P. XI). *Average dose.*— $2\frac{1}{2}$  drachms.**  
Wild cherry bark 15, sucrose 80, glycerin 5, alcohol 2, water to 100.

**[P1] Tinctura Pruni Serotinæ (B.P.C.). *Syn.* TINCTURA PRUNI  
VIRGINIANÆ.**

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.). 1 in 5.

**Stillingia (B.P.C.). *Syn.* QUEEN'S ROOT, YAW ROOT.**

*Dose.*— $\frac{1}{2}$  to 1 drachm (1 to 2 g.).

The dried root of *Stillingia sylvatica* (Euphorbiaceæ). Contains volatile oil.  
Large doses emetic, cathartic; small doses sialagogue and expectorant.

## SENNÆ

**Sennæ Folium** (B.P.). *Syn.* SENNA (U.S.P. XI).

*Dose.*—10 to 30 grains (0·6 to 2 g.).

The dried leaflets of *Cassia acutifolia* (Alexandrian) or *C. angustifolia* (East Indian or Tinnevely) (Leguminosæ). *P. Helv. V* and *P. Dan.* recognise *C. angustifolia* only. Contains aloëmodin, kempferol, isorhamnetin, etc.

*Uses.* Senna is a safe, useful purgative for simple constipation, but owing to its tendency to gripe it is usually given with carminatives. Confection of senna is a suitable laxative for children and delicate persons, and is especially valuable in hæmorrhoids. Preparations made from the fruit are said to be less griping than those from the leaf, and infusion of senna pods is a popular and harmless purgative for regular use.

**Confectio Sennæ** (B.P.). *Syn.* LENITIVE ELECTUARY.

*Dose.*—1 to 2 drachms (4 to 8 g.).

Contains senna 10% with coriander, figs, tamarind, cassia, prunes, extract of liquorice, sugar and water. The use of coriander oil instead of the fruit has been suggested.

**Confectio Sennæ Composita** (C.X.H.). Powdered jalap 3 gr., senna leaf 3 gr., sublimed sulphur 3 gr., black treacle to 60 gr.

**Confectio Sennæ et Sulphuris** (B.P.C.).

*Dose.*—1 to 2 drachms (4 to 8 g.).

Equal parts of confection of senna and confection of sulphur.

**Fluidextractum Sennæ** (U.S.P. XI). *Average dose.*—30 minims (2 ml.). 1 ml. represents 1 g. of senna leaf.

**Syrupus Sennæ** (U.S.P. XI). *Average dose.*—2 drachms (8 ml.).

Fluidextract of senna 25, oil of coriander 0·5, sucrose 63·5 in water to 100.

**Tinctura Sennæ Composita** (B.P.C.).

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.) for repeated administration; 2 to 4 drachms (8 to 16 ml.) for a single administration.

Senna leaf 1 in 5, with caraway and coriander.

**Sennæ Fructus** (B.P., *P. Helv. V*). *Syn.* SENNA POD.

*Dose.*—10 to 30 grains (0·6 to 2 g.); corresponding to about 4 to 12 pods.

The dried ripe fruits of either Alexandrian or Tinnevely senna.

*P. Dan.* recognises *C. angustifolia* only. These are stronger than the leaves and preparations made without crushing the seeds are believed to be less griping than those from the leaf.

**Elisir Sennæ** (B.P.C.). *Syn.* LIQUOR SENNÆ LEGUMINORUM DULCIS.

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

A flavoured preparation containing 50% v/v of liquid extract of senna.

**Extractum Sennæ Liquidum** (B.P.).

*Dose.*—10 to 30 minims (0·6 to 2 ml.).

1 in 1, by maceration in chloroform water, evaporation, and addition of alcohol.

**Infusum Sennæ Concentratum** (B.P.).

*Dose.*— $\frac{1}{2}$  to 2 drachms (2 to 8 ml.).

1 in  $1\frac{1}{2}$  by percolation with alcohol 20% and addition of 1 in  $12\frac{1}{2}$  of strong tincture of ginger.

**Infusum Sennæ Recens** (B.P.).

*Dose.*— $\frac{1}{2}$  to 2 ounces (15 to 60 ml.).

Senna 1 in 10 and ginger 1 in 200.

**Mistura Sennæ Composita** (B.P.). *Syn.* BLACK DRAUGHT.

*Dose.*—1 to 2 ounces (30 to 60 ml.).

Magnesium sulphate 1 in 4 with liquid extract of liquorice, compound tincture of cardamom, aromatic spirit of ammonia and infusion of senna.

**Syrupus Sennæ** (B.P.).

*Dose.*— $\frac{1}{2}$  to 2 drachms (2 to 8 ml.).

Liquid extract of senna 25% v/v with oil of coriander, sucrose and water.

**Lixen** (Allen & Hanburys, London). Elixir of senna pods. 1 drachm = 10 large senna pods. Also in lozenges and pastilles.

**Baptisia** (B.P.C.). *Syn.* WILD INDIGO ROOT.

The dried root of *B. tinctoria* (Leguminosæ). Has laxative properties and has been given as a decoction.

**Tinctura Baptisiæ** (B.P.C.). 1 in 10. Occasionally added to mouth-washes for its saponin content.

**Baptisin.** *Dose.*—1 to 5 grains. An extractive from baptisia; in small doses laxative, in large doses cathartic. The mother tincture of baptisia (homœopathic) has a reputation for treatment of boils.

**Ficus** (B.P.C.). *Syn.* FIG, CARICA (*P. Helv. V*).

The dried fruit of *F. Carica* (Moraceæ), a mild laxative.

**Syrupus Ficorum** (B.P.C.).

*Dose.*— $\frac{1}{2}$  to 2 drachms (2 to 8 ml.).

Is prepared by dissolving sucrose in an aqueous decoction.

**Syrupus Ficorum Compositus** (B.P.C.). *Syn.* SYRUPUS FICORUM AROMATICUS.

*Dose.*— $\frac{1}{2}$  to 2 drachms (2 to 8 ml.).

Contains compound tincture of rhubarb, liquid extract of senna, elixir of cascara sagrada and syrup of figs.

**Ficin.** The sap of the fig tree, used by the natives of S. America for the treatment of intestinal parasites, has recently been investigated as an anthelmintic, and has been found to remove about 80% of *Trichuris*, as compared with the 20 or 25% removed by most other substances and the 40 or 50% removed by hexyl-resorcinol. The active principle is a proteolytic enzyme which digests the parasites. It is non-irritating and non-toxic if no lesion of the intestinal tract is present, in which case it causes dangerous erosion of the mucous membrane.—P. D. Lamson and co-workers, *J. Amer. med. Ass.*, ii/1932, 293.

**Morus** (B.P.C.). *Syn.* MÛRE (*Fr. Cx.*).

Mulberry is the fresh ripe fruit of *M. nigra* (Moraceæ). Mulberry juice is slightly laxative and expectorant.

**Syrupus Mori** (B.P.C.).

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

A solution of sucrose in mulberry juice.

**Prunus** (B.P.C.). Prune is the dried ripe fruit of *P. domestica* var. *Juliana* (Rosaceæ). Has laxative properties.

**Cerasus.** Red cherry is the fruit of *Prunus Cerasus* var. *caproniana*.

**Syrupus Cerasi** (B.P.C.).

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

A solution of sucrose in red cherry juice. A flavouring and colouring agent.

**Ribes Nigrum.** The fresh ripe fruit of the black currant.

**Syrupus Ribis Nigri** (B.P.C.).

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.). A solution of sucrose in the juice expressed from a mixture of black currants and red cherries.

**Ribes Rubrum.** The fresh ripe fruit of the red currant.

**Syrupus Ribis Rubri** (B.P.C.). *Syn.* SIROP DE GROSEILLE (*Fr. Cx.*).

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.). A solution of sucrose in the juice expressed from a mixture of red currants and red cherries.

**Tamarindus** (B.P.). *Syn.* WEST INDIAN TAMARINDS.

The fruits of *Tamarindus indica* (Leguminosæ) freed from the brittle outer part of the pericarp and preserved with sugar. Occurs as a reddish-brown moist sugary mass. Contains tartaric acid, potassium acid tartrate and about 30% of sugar. Is also imported pressed into a solid mass as pulp (*Pulpa Tamarindi cruda*, *P. Helv. V*). A mild laxative.

## SINAPIS NIGRA

*B.P.C., Fr. Cx.*

*Syn.* SEMEN SINAPIS (*P. Helv. V, F.E. VIII, P. Ital. V, P. Belg. IV*).

Black mustard is the dried ripe seeds of *Brassica sinapoides* (Cruciferæ). *U.S.P. XI* allows *B. sinapoides* also *B. juncea* and varieties of these species.

They contain the glycoside, sinigrin, and the enzyme, myrosin, which interact in the presence of water to yield allyl isothiocyanate (0.6 to 1%).

(*SINAPIS ALBA* is obtained from *B. alba*. It yields no allyl isothiocyanate. *BATH MUSTARD* is powdered mustard from which the seed coats have not been completely removed. *MUSTARD BRAN* consists usually of the seed coats of black mustard. *MUSTARD FLOUR* consists of powdered black and white seeds from which the seed coats have been largely removed).

*Uses.* As an emetic a tablespoonful in half a pint of warm water. In small doses is a stomachic and appetiser. Externally, a counter-irritant when applied as a poultice, or added to hot water and used as a foot-bath. It may blister tender skins.

**Balneum Sinapis** (*B.P.C.*). Contains 12 oz. of bath mustard per 30 gallons.

**Cataplasma Sinapis** (*B.P.C.*). Mustard flour 2% in linseed poultice.

**Emplastrum Sinapis** (*U.S.P. XI*). A spread plaster on paper, cloth or other material, prepared with oil-free black mustard and rubber solution; each sq. cm. contains at least 0.025 g. of the mustard. It should be applied after moistening with tepid water. **Charta Sinapisata** (*P. Helv. V*) contains 0.03% of  $C_2H_5NCS$ . Is also official in *P. Dan.*

**Oleum Sinapis Expressum** (*B.P.C.*). *Syn.* BLACK MUSTARD OIL.

Obtained by expression from black mustard seeds; the average content is about 26%. A brownish-yellow or greenish-brown oil used as a mild rubefacient. WHITE MUSTARD SEED OIL, from the seeds of *B. alba*, is used for lubricating and for burning.

**Oleum Sinapis Volatile** (*B.P.C., U.S.P. XI, P. Helv. V*). *Syn.* ALLYL ISOETHIOCYANATE, ESSENCE OF MUSTARD (*Fr. Cx.*).

*Dose.*—No dose given in *B.P.C.* *U.S.P. XI* has average dose  $\frac{1}{2}$  minim.

Consists chiefly of allyl isothiocyanate,  $C_2H_5NCS$ , and may be prepared synthetically or distilled from black mustard seeds after expression of the fixed oil and maceration in tepid water to allow

interaction between the glycoside, sinigrin (potassium myronate), and the enzyme, myrosin.

$\alpha$ -Naphthyl isothiocyanate ( $C_{10}H_7NCS$ ) is a white, crystalline substance, m.p.  $55.5^\circ$ , b.p.  $142^\circ$ , slightly soluble in water, but soluble in kerosene up to 12%. It has a slight odour and is non-staining, and is loosely called mustard oil. Alone it is not sufficiently poisonous to flies for an insecticide, but mixed with pyrethrum it has a satisfactory toxic action. It is said that the addition of 1% of  $\alpha$ -naphthyl isothiocyanate to an insecticide allows the elimination of about 60% of the pyrethrum whilst maintaining the desired toxic effect.—per *Pharm. J.*, i/1940, 41.

**Linimentum Sinapis (B.P.C.).**

Volatile oil of mustard 3.5% in a castor oil, camphor and alcohol mixture.

**Spiritus Sinapis (P.G. VI).** Volatile oil of mustard 1, alcohol (90%) 49.

**Thiosinamina (B.P.C., Fr. Cx.).** *Syn.* RHODALLIN, ALLYL-THIOUREA, ALLYL-SULPHOCARBAMIDE.  $CS(NH_2)NHC_3H_5 = 116.1$ .

*Dose.*—Internally,  $\frac{1}{2}$  grain gradually increased to  $1\frac{1}{2}$  grains (0.03 to 0.1 g.) (with caution—in capsule or alcoholic solution). Hypodermically 1 to  $1\frac{1}{2}$  grains as *Injectio Thiosinaminæ et Sodii Salicylatis*.

White crystals, usually with a slight garlic-like odour, and having a bitter taste. M.p.  $72^\circ$  to  $74^\circ$ . May be obtained by the interaction of volatile oil of mustard, alcohol and ammonia solution.

**Soluble** 1 in 17 of water, about 1 in 2 of alcohol 90%, and in ether. Readily soluble in solutions of borax, urethane, benzoates, cinnamates, etc.

**Uses.** To some extent internally, but chiefly by injection (*vide infra*) with sodium salicylate, for absorbing fibrous and scar tissue. Has been used for keloid and in scleroderma. It sometimes gives rise to toxic effects, such as nausea, vomiting, headache, and fever. In ophthalmology it has been used in corneal opacity, corneal scars, choroiditis and other conditions.

**TINNITUS AURIUM** has been treated by 5% aqueous solution hypodermically with improvement, dose being increased from 6 to 35 m., also a 10% solution and a 20% glycerin solution. Should be tried before operating on the middle ear or labyrinth for this trouble.

**PERICARDIAL ADHESIONS** have been treated by 3-gr. doses in 80 m. of water every other day in the flanks for 30 days.

**Injectio Thiosinaminæ et Sodii Salicylatis (B.P.C.).**

*Dose.*—8 to 15 minims (0.5 to 1 g.).

Contains 10% w/v of thiosinamine dissolved with aid of sodium salicylate in diluted glycerin.

**Uses.** For relaxing scar tissue, in strictures of the gullet, urethra and rectum, in stenosis of the pylorus, rheumatoid arthritis, Dupuytren's contraction and eye affections (corneal infiltrations). It should be injected in the neighbourhood of the tissues to be absorbed, and the injections continued for several months. Massage and stretching or the use of bougies in appropriate cases may be of value. Also in middle-ear disease and for tinnitus (but the "remote action" in such is doubtful), and in pleural adhesions, injected locally or into the gluteal muscles once or twice weekly according to severity of case. It may be of value in arteriosclerosis and chronic rheumatism.

**Cicatricine** (*Martindale, London*). Injection of thiosinamine and phenazone containing per ml. 3 gr. of thiosinamine, 5 gr. of phenazone and  $\frac{1}{10}$  gr. of benzamine lactate. A non-toxic, non-irritating injection for the treatment of cicatricial tissue.

**Fibrolysin** (*Merck, Darmstadt; Martindale, London*). Thiosinamine sodium salicylate. Supplied in ampoules (2 ml.), suppositories (0.3 g.) and lymph tubes (for the eye). *Dose*.—1 ampoule intragluteally every 2nd or 3rd day, 1 suppository at night, or 1 to 3 drops into the eye thrice daily.

**Thiosinaminæ et Æthylis Iodidum.** *Syn. and Prop. Name.* THIODIN, TIODINE (*Cognet, Paris; Roberts, London*).  $\text{CS}(\text{NH}_2\text{C}_2\text{H}_5\text{I})\text{NHC}_3\text{H}_5 = 272.1$ .

*Dose*.—1 to 4 grains (0.06 to 0.25 g.) daily by mouth; 3 to 6 grains (0.2 to 0.4 g.) three times weekly by injection.

Prepared by heating thiosinamine and ethyl iodide under a reflux condenser. Forms white crystals melting at about 70°.

*Soluble* 1 in 10 of water and 1 in 1 of alcohol 90%.

*Used* for the same purposes as thiosinamine, also given internally in intractable rheumatoid arthritis. Skin rashes may follow its oral administration. A saline draught should be given each morning during administration; alcohol and red meat should be avoided, and plenty of water drunk.

**ACTINOMYCOSIS.** 5 cases treated hypodermically with rapid and complete success.—T. G. Moorhead, *Brit. med. J.*, i/1929, 419.

**Iodolysin** (*Allen & Hanburys, London*). A similar preparation, stated to contain 43% thiosinamine and 47% of I. Iodolysin solution for oral use, 30 m. containing 2 gr. Iodolysin; also *Injection* (hypodermic) 15 m. containing 2 gr. *Ointment and Pigment* are also prepared. To soften cicatrices and promote absorption of fibrous tissue. Of value in rheumatoid arthritis.

**Armoracia** (*B.P.C.*). Horseradish is the fresh root of *Cochlearia Armoracia* (*Cruciferae*). Contains sinigrin (potassium myronate) and the enzyme myrosin, which react in the presence of water to give allyl isothiocyanate. The infusion, 1 in 20, has been given as a stimulant.

**Spiritus Armoracæ Compositus** (*B.P.C.*).

*Dose*.—1 to 2 drachms (4 to 8 ml.).

A distilled spirit representing 1 in 8 of horseradish. Administered as a carminative.

**Mezereum** (*B.P.C., P. Helv. V.*). *Syn.* MEZEREON.

*Dose*.—8 grains (0.5 g.). The dried bark of *Daphne Mezereum* (*Thymelæaceæ*) and other species. Contains an acrid resin and a bitter glycoside (daphnin). At one time had a reputation as an alternative in syphilis, chronic rheumatism, etc., but is now seldom given internally except as an ingredient of compound decoction of sarsaparilla. Externally it has been employed as a stimulant and vesicant.

## SODIUM

Na = 22.997.

*Notes on other sodium salts are included under the corresponding acids (see Index).*

**Liquor Sodii Æthylatis** (*B.P.C.*).

A 1 in 20 solution of sodium in dehydrated alcohol, the latter being cooled by a stream of cold water; contains 18% of  $\text{C}_2\text{H}_5\text{ONa}$ . Rapidly becomes brown.

*Uses.* A powerful caustic and has been used for the treatment of nævi, warts and lupus; also in hypertrichosis. It should always



be used in alcoholic solution and applied with a glass rod on 2 or 3 successive days. No water should be allowed to touch the part.

**Liquor Sodii Methylatis.**

Is prepared on lines similar to the above, employing methyl instead of ethyl alcohol.

**Sodii Bicarbonas** (*B.P., U.S.P. XI, P. Helv. V, Fr. Cx., etc.*). *Syn.* SODII CARBONAS ACIDUS, SAL DE VICHY (*F.E. VIII*).  $\text{NaHCO}_3 = 84.00$ .

*Dose.*—15 to 60 grains (1 to 4 g.). *U.S.P. XI* average dose 15 grains.

Occurs in small white crystals or powder. 20 parts are neutralised by 17 of citric or 18 of tartaric acid.

**Soluble** 1 in 11 of water; insoluble in alcohol 90%. A 1.35% *w/v* solution is isotonic with blood.

Solutions for *intravenous injection* should be prepared by adding sodium bicarbonate aseptically to cold, freshly prepared sterilised water and shaking to dissolve.—O. Turner, *Trans. R. Soc. trop. Med. Hyg.*, 1940, 34, 112.

**Incompatible** with acids and acid salts, and with metallic and alkaloidal salts. Bismuth, magnesium and lithium benzoates and salicylates are incompatible with sodium bicarbonate. It is also incompatible with aspirin.

**Uses.** Sodium bicarbonate is mainly used as an antacid. In particular it gives prompt relief in simple hyperchlorhydria, flatulent dyspepsia and heartburn. An objection to its use, however, is that the initial reduction of gastric secretion is followed by an increased acidity due to the evolution of carbon dioxide, and it is now more usual to give it in association with other antacids and bismuth. In order to inhibit excessive secretion in the stomach and to stimulate appetite it is given with bitter stomachics, such as gentian or rhubarb, thirty minutes before meals. In acidosis, especially that associated with diabetes, its use either by the mouth, or intravenously in 5% solution (500 ml. in 30 minutes), is of great value. Large doses (up to 7 g. daily) may also be employed to render the urine alkaline in the treatment of infections of the urinary tract, such as pyelitis and cystitis, and in acute nephritis, and alkalisation by sodium bicarbonate, either orally or intravenously, to the limit of toleration, is said to be of great value in blackwater fever. In the cyclical vomiting of children and in the toxæmia of pregnancy, large doses given in association with dextrose are of great value.

Sodium bicarbonate is also employed for its action in dissolving mucus, and it may be used as a mouth wash or gargle (1 to 4%), or as a liquefying expectorant, in all kinds of catarrhal conditions, *e.g.*, bronchial catarrh and bronchitis; in gastric catarrh and dilatation, lavage with a 1% solution is an efficient treatment.

Applied locally to the skin, weak solutions (1 in 150) relieve the irritation of urticaria, eczema and dermatitis, and a 2% solution in water is used as an eye lotion. The use of lotions or eye ointments containing sodium bicarbonate are especially recommended for the treatment of burns of the eye due to contamination by mustard gas.

Sodium bicarbonate is particularly unsatisfactory as an antacid. It is soluble in water (the ideal antacid should be insoluble); it is irritating in high concentrations; after an initial neutralisation of hydrochloric acid it causes a secondary rise in acidity to heights not previously reached; in fact it is now recognised to be the most potent stimulus to acid production known, apart from histamine. It has the further disadvantage of causing an evolution of carbon dioxide and a rise in intragastric tension, which may prove dangerous in the presence of an ulcer. It is rapidly absorbed and when used in large doses, or over long periods, may give rise to alkalosis, especially when there is hepatic or renal insufficiency. It should not be used as an antacid in the treatment of peptic ulcer, though an occasional dose for the relief of pain of exceptional severity may be necessary.—T. L. Hardy, *Practitioner*, i/1937, 436.

**BLACKWATER FEVER.** Sodium bicarbonate intravenously, 10 to 20 ounces of strength 150 gr. to the pint curtails duration of attack, prevents blockage of kidney tubules, and avoids suppression of urine.—W. E. Cooke and H. Willoughby, *Lancet*, i/1929, 334.

Sodium bicarbonate orally and the citrates or lemonade. Sodium bicarbonate 10 g., glucose 10 g., given in 1000 ml. initially and large amounts (up to 21 g. in 24 hours) repeatedly during treatment. Quinine could be taken when the urine was kept alkaline.—C. C. Chesterman, *Lancet*, i/1929, 1355. *See also* C. P. Downison, ii/1929, 47.

**DIABETIC COMA.** In two cases of diabetic coma with severe acidosis, in which insulin treatment did not rapidly bring about the expected improvement, intravenous injection of 2 litres of an isotonic solution (1.3%) of sodium bicarbonate immediately relieved the coma. It is generally necessary to determine the plasma-bicarbonate values several times during the first 24 hours.—E. Kirk, *Lancet*, i/1939, 505.

**ECZEMA.** Obstinate cases cured by daily bath of 2 lb. of sodium bicarbonate to 20 gallons of water, with change of linen and an ounce of magnesium hydrate twice daily. A case of 18 years' standing cleared up in 3 days.—S. A. Leader, *Brit. med. J.*, ii/1931, 323.

**Eye Ointment for Gas Poisoning.** The following ointment should be instilled at once. Sodium bicarbonate 3%, distilled water 10%, wool fat 10%, soft paraffin to 100%. After 24 hours it should be replaced by 10% boric acid ointment. The patient can apply the ointment by pulling down the lower lid, laying the ointment (preferably supplied in tubes) along the lower fornix, looking down and then closing the eye. The eyes should be kept bandaged.—R. L. Rea, *Brit. med. J.*, ii/1939, 883.

Eye salve to combat the effect of gas:—Sodium biborate (impalpable powder) 1 part; purified sodium bicarbonate 2 parts, distilled water and lanolin of each 10 parts, white Vaseline to 100 parts.—Gemeinhardt, per *J. Amer. pharm. Ass.*, 1938, 322.

**Balneum Effervescens (B.P.C.).** Sodium bicarbonate 16 oz. and sodium acid sulphate 8 oz. per 30-gallon bath.

**Balneum Effervescens cum Chlorido (B.P.C.)** is the same with the addition of sodium chloride 48 oz. and calcium chloride 8 oz.

**Bain dit de Vichy.**

Sodium bicarbonate 500 g., dissolve in the bath at time of use.

**Collyrium Sodii Bicarbonatis (B.P.C.).** 2% w/v.

**Gargarisma Sodii Bicarbonatis (B.P.C.).** 5% w/v.

**Gutta Sodii Bicarbonatis (T.H.).** Sodium bicarbonate 15 gr., phenol 1 gr., glycerin 2 dr., water to  $\frac{1}{2}$  oz. For softening wax in the ear before syringing.

**Factory Eye Drops No. 2.** Sodium bicarbonate 15 gr., water to 1 oz.

**Mistura Sodii Bicarbonatis Aromatica (B.P.C.).**

*Syn.* MISTURA CARMINATIVA.

*Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.).

Contains sodium bicarbonate 10 gr. per oz. with aromatic spirit of ammonia, compound tincture of cardamom, glycerin and dill water.

**Mist. Carminat. (N.I.F.).** Sodium bicarbonate 10 gr., light magnesium carbonate 5 gr., aromatic tincture of cardamom 5 m., water to  $\frac{1}{2}$  oz.

**Mistura Carminativa** (*Gt. Orm. H.*). (Dose for 1 year old child.)

Sodium bicarbonate 1½ gr., aromatic spirit of ammonia 1½ m., glycerin 5 m., peppermint water to 1 dr.

**Nebula Alkalina** (*T.H.*). Sodium bicarbonate 15 gr., borax 15 gr., phenol 4 gr., glycerin 45 m., water 1 oz. **Dobell's Solution** is approx. half this strength.

**Nebula Alkalina Composita** (*B.P.C.*).

Sodium bicarbonate and borax of each 1.5% w/v, and phenol 0.75% w/v, in glycerin and water.

**Pulv. Antacid.** (*N.I.F.*). *Average dose.*—30 grains.

Sodium bicarbonate, heavy magnesium carbonate and chalk, of each 320 grains, oil of peppermint 2 m.

**Sodii Citro-Tartras Effervescens** (*B.P.C.*).

*Dose.*—1 to 2 drachms (4 to 8 g.).

Effervescent granules containing sodium bicarbonate, citric and tartaric acids.

**Solvellæ Nasal. Alk.** (*N.I.F.*). *Syn.* TAB. NASAL ALK. Sodium bicarbonate 5 gr., thymol  $\frac{30}{100}$  gr., borax 5 gr. 1 to be dissolved in 4 tablespoonfuls of warm water.

**Tabellæ Sodii Bicarbonatis Compositæ** (*B.P.C.*).

*Syn.* SODA MINT TABLETS. *Dose.*—1 to 4 tablets.

Contain sodium bicarbonate 5 gr., ammonium bicarbonate  $\frac{1}{2}$  gr., saccharin and oil of peppermint.

The formulæ for compound sodium bicarbonate and compound ginger tablets are impracticable owing to the volatility of the ammonium bicarbonate, the omission of which is recommended. In addition it is suggested that the names "soda mint" and "ginger mint" should be reserved for those tablets which it has been the custom of the trade to supply, consisting of sodium bicarbonate and oil of peppermint for soda mints, with the addition of oleo-resin of ginger for ginger mints.—H. Burlinson, *Quart. J. Pharm.*, 1938, 518.

Two samples of the tablets were not made in accordance with the *B.P.C.* formula. These are further instances of the unfortunate confusion arising from the fact that the name "soda mint" has been applied to tablets made up to different formulæ. It is surely not impossible to arrange that a specific name should always connote the same mixture of ingredients and to ensure that a customer will always be supplied with the same article whenever he makes his purchase.—H. H. Bagnall, per *Analyst*, 1939, 878.

**Tabellæ Zingiberis Compositæ** (*B.P.C.*).

*Syn.* GINGER MINT TABLETS. *Dose.*—1 or 2 tablets.

Sodium bicarbonate 5 gr., oleoresin of ginger  $\frac{10}{100}$  gr., ammonium bicarbonate, saccharin and oil of peppermint.

**Sodii Carbonas** (*B.P., P. Helv. V, Fr. Cx., etc.*).

$\text{Na}_2\text{CO}_3 \cdot 10\text{H}_2\text{O} = 286.2$ .

*Dose.*—5 to 15 grains (0.3 to 1 g.).

Rhombic crystals efflorescing in air.

**Soluble** 1 in 2 of water, 1 in 1 of glycerin; insoluble in alcohol 90%.

**Uses.** Employed in the preparation of alkaline baths for use in scaly skin diseases. A lotion, 2 gr. to the ounce, relieves eczema. 1% is used as mouth wash or nasal douche. Instruments are boiled in a 1% solution to sterilise and to prevent rusting.

**Balneum Alkalinum** (*B.P.C.*) contains 5 oz. of sodium carbonate per 30 gallons.

**Liquor Sodii Carbonatis** (*R.L.O.H.*).

To sterilise instruments: sodium carbonate 1 oz., sterile water to 80 oz. Boil Graefe knives  $\frac{1}{2}$  minute, other instruments 3 minutes.

**Sodii Carbonas Exsiccatus** (*B.P., P. Helv. V, Fr. Cx.*).  
 $\text{Na}_2\text{CO}_3 = 106.0$ .

*Dose.*—2 to 5 grains (0.12 to 0.3 g.).

Approximately 106 of the exsiccated salt are obtained from 286 of the crystals.

**Sodii Carbonas Monohydratus** (*U.S.P. XI, P. Helv. V*).  
 $\text{Na}_2\text{CO}_3 \cdot \text{H}_2\text{O} = 124.0$ . *U.S.P. XI* average dose 4 grains. Is known in commerce as concentrated "crystal soda," and used as a bath salt and water softener. It occurs in small silky crystals.

**Sodii Sesquicarbonas**.  $\text{Na}_2\text{CO}_3 \cdot \text{NaHCO}_3 \cdot 2\text{H}_2\text{O}$ . In silky crystals or as a white powder. Is sometimes used in the preparation of bath salts.

**Sodii Chloras** (*B.P.C., Fr. Cx., F.E. VIII*).  $\text{NaClO}_3 = 106.5$ .  
*Dose.*—5 to 10 grains (0.3 to 0.6 g.).

**Caution.** Not to be rubbed with combustible substances. Colourless crystals or crystalline powder with saline taste.

**Soluble** 1 in less than 2 parts of water, about 1 in 100 of alcohol 90%, and 1 in 5 of glycerin.

It closely resembles potassium chlorate in its properties, and is used in stomatitis, sore throat, etc., in the form of a gargle or lozenge. It is used in some non-poisonous weed-killers.

Sodium chlorate is a highly effective weed-killer, a 1% solution being sufficiently strong. Its toxic action, which begins after absorption by the plant, remains in the ground for several months. Precautions should be taken against using wooden stirrers, etc., in preparing the solution, since such material, saturated with sodium chlorate solution and allowed to dry, becomes highly inflammable.—*Pharm. J.*, i/1938, 381.

**Sodii Hydroxidum** (*B.P., U.S.P. XI, P. Helv. V, P. Dan.*).  
 Syn. SODA CAUSTICA.  $\text{NaOH} = 40.00$ .

[P2] "Sodium hydroxide."

[S3] "Sodium hydroxide—in substances containing less than twelve per cent. of sodium hydroxide."

[S6] "Sodium hydroxide—specify proportion as the proportion of sodium monoxide ( $\text{Na}_2\text{O}$ ) which the preparation would be calculated to contain on the assumption that the sodium hydroxide in the preparation had been wholly converted into sodium monoxide."

[S7] Sodium hydroxide and articles containing it must be labelled "Caution. This substance is caustic."

In fused masses, moulded sticks or white scales, containing not less than 95% of total alkali calculated as  $\text{NaOH}$ . It has similar properties to those of potassium hydroxide.

**Soluble** 1 in 1 of water, with the evolution of much heat; also soluble in alcohol and glycerin.

**Antidotes.** Treat as for poisoning by ammonia, see p. 180.

Eight cases of poisoning (4 suicides) in Cyprus during 1933 with 6 fatalities. The fatal dose varied from 5 to 60 grammes. It is largely used for domestic washing purposes.—S. G. Willmott and M. Gosden, *Brit. med. J.*, i/1934, 1022. See also *Lancet*, ii/1933, 413.

**Sodii Nitris** (*B.P., U.S.P. XI, Fr. Cx., P. Helv. V*).  
 $\text{NaNO}_2 = 69.0$ .

*Dose.*— $\frac{1}{2}$  to 2 grains (0.03 to 0.12 g.).

Is obtained by reduction of sodium nitrate by fusing it with lead.

In white or slightly yellow deliquescent, crystalline granules, with a cooling saline taste.

**Soluble** 1 in  $1\frac{1}{2}$  of water, 1 in 50 of alcohol 90%.

**Antidotes.** Treat as for poisoning by amyl nitrite, see p. 160.

Deaths of three members of one family at Middlesbrough 2 hours after consuming sodium nitrite used in error for salt. The first fatal case of nitrite poisoning in this country.—*Pharm. J.*, ii/1936, 214. See also *Lancet*, ii/1936, 1153.

**Uses.** Has a vasodilator action similar to that of amyl nitrite, but is slower and much more prolonged (1 to 2 hours). Tolerance tends to be established and dosage should be intermittent. Raised arterial tension when dangerous is well treated by  $\frac{1}{2}$ -grain doses, gradually increased to 4 or 5 grains. Attacks of asthma may be warded off by sodium nitrite  $\frac{1}{2}$  gr. with sodium iodide 3 gr. taken (e.g. in a tablet) every 2 or 3 hours. A 2-gr. dose of sodium nitrite with 3 gr. of sodium iodide has been advocated for paroxysmal pain due to aortic insufficiency.

It does not fulfil the requirements of the treatment of arterial hypertension in that it has no constant and sustained action, does not act by dilating the arterioles all over the constricted areas, may give rise to unpleasant symptoms and side-effects, does not maintain the normal functions of the heart and kidneys, and may depress renal activity.—S. Weiss and L. B. Ellis, per *Brit. med. J. Epit.*, ii/1933, 72.

**RETROBULAR NEURITIS.** Eight out of 9 cases received benefit, shown by increased visual acuity and by diminution of scotomata, from intravenous injections of 10% sodium nitrite, in doses ranging from 0.04 to 0.1 g. injected daily over a period of about a week.—W. F. Duggan, per *Med. Pr.*, ii/1936, 539.

**TOBACCO AMBLYOPIA.** 24 cases of tobacco amblyopia without optic atrophy received from 6 to 10 intravenous injections of sodium nitrite (100 mg.), which were given daily when possible. Two patients were not improved and one was not adequately treated. The remaining 21 attained vision of 20/30, or better, in one or both eyes in an average time of 18.4 days, and 12 attained vision of 20/20 in an average time of 30 days. Five of the patients smoked during the period of treatment, and the average time during which they obtained vision of 20/30, or better, was 36 days. For the 16 patients that abstained from smoking the average time for the same improvement was 12 days, and 10 of the patients attained this result within 7 days. Daily injections were found most effective, and patients who had used both alcohol and tobacco improved more rapidly than those who had used only tobacco. The treatment is based on the hypothesis that tobacco amblyopia is due primarily to a vascular spasm in the visual pathway.—W. F. Duggan, *Arch. Ophthalm.*, 1935, 13, 1059. (See also acetylcholine.)

**Pulvis Sodii Nitritus Compositus.**—Brunton.

Sodium nitrite  $\frac{1}{2}$  to 2 gr., potassium nitrate 10 to 20 gr., and sometimes potassium bicarbonate 10 gr.—in a tumbler of water every morning to reduce blood pressure.

**P1] Tabellæ Sodii Nitritus Compositæ (B.P.C.).**

*Dose.*—1 or 2.

Sodium nitrite  $\frac{1}{2}$  gr., diluted erythrityl tetranitrate  $\frac{1}{2}$  gr., ammonium hippurate 1 gr.

**Liquor Æthylis Nitritus (B.P.C.).**

*Dose.*— $\frac{1}{4}$  to 1 drachm (1 to 4 ml.). Should be directed to be added to a small quantity of water at the time of taking.

A solution of ethyl nitrite, 2.5 to 3% w/w (equivalent to 2 to 2.5% w/v) in a mixture of dehydrated alcohol and glycerin.

**Spiritus Ætheris Nitrosi (B.P.).***Syn.* SWEET SPIRIT OF NITRE.*Dose.*—15 to 60 minims (1 to 4 ml.).

An alcoholic solution containing ethyl nitrite (1.25 to 2.5% w/v), aldehyde and other substances.

Any loss of strength in this is generally due to volatilisation of the ethyl nitrite alone. Only direct sunlight has any effect in inducing decomposition, and this can be prevented by storing in amber bottles with greased stoppers.—*R. Wright, Pharm. J.*, i/1926, 256.

**Incompatible** with potassium iodide, also with phenazone unless previously neutralised with sodium bicarbonate; also incompatible with salicylates and ferrous sulphate.

**Uses.** Diaphoretic, diuretic, and stimulant. Relieves the spasm and pain of asthma, dysmenorrhœa, angina pectoris; also the pain of the passage of renal calculi and gall-stones.

**Spiritus Æthylis Nitritus (U.S.P. XI).** *Average dose.*—30 minims (2 ml.). An alcoholic solution containing 3.5 to 4.5% w/w of  $C_2H_5ONO$ .

**STRAMONIUM**

*B.P., U.S.P. XI, Fr. Cx., P. Helv. V, etc.*

[P1] "*Alkaloids, the following; their salts, simple or complex:—atropine; hyoscyne; hyoscyamine; solanaceous alkaloids not otherwise included in this List.*"

[S1] "*Alkaloids, the following; their salts, simple or complex:—Atropine except substances containing less than 0.15% of atropine; hyoscyne except substances containing less than 0.15% of hyoscyne; hyoscyamine except substances containing less than 0.15% of hyoscyamine; solanaceous alkaloids not otherwise included in this Schedule, except substances containing less than 0.15% of solanaceous alkaloids calculated as hyoscyamine.*"

[S3] "*Alkaloids—Solanaceous alkaloids—in stramonium contained in preparations for the relief of asthma in the form of cigarettes, smoking mixtures or fumigants.*"

[S6] "*Alkaloids—Solanaceous alkaloids not otherwise included in the Poisons List—specify proportion as the proportion of any one of the solanaceous alkaloids that the preparation would be calculated to contain on the assumption that all the solanaceous alkaloids in the preparation were that alkaloid.*"

*Dose.*— $\frac{1}{4}$  to 3 grains (0.03 to 0.2 g.); 3 grains contains about  $\frac{1}{15}$  gr. of alkaloids. *U.S.P. XI* average dose  $1\frac{1}{2}$  grains, *Fr. Cx.* and *P. Helv. V* have max. single dose approx. 5 grains, max. in 24 hours approx. 15 grains.

Dried leaves and flowering tops of *Datura Stramonium* (*syn.* THORNAPPLE) and of *D. tatula* (*Solanacæ*) containing not less than 0.25% of alkaloids calculated as hyoscyamine. The principal alkaloid is hyoscyamine, with possibly hyoscyne and a little atropine.

A key for distinguishing various species of *Datura*.—H. A. Timmerman, *Pharm. J.*, i/1927, 574.

**Antidotes.** Treat as for poisoning by atropine, see p. 237.

**Uses.** Its action is similar to that of belladonna leaf, and it may be employed for the same purposes. Its properties are those of the alkaloid hyoscyamine. It is employed in asthma to relieve the spasm of the bronchial tubes. The leaf is smoked in cigarettes and is an ingredient of powders intended to be burnt for the relief of asthma. It is a useful and convenient drug for the symptomatic treatment of post-encephalitic parkinsonism and it may be taken without interruption over long periods without harmful effect.

**CHRONIC ENCEPHALITIC PARKINSONISM.** Results equal to those from hyoscine hypodermically are obtained by giving stramonium extract *per os* in dose of 0.25 g. to 1 g. or more thrice daily, the average dose being 0.75 g. No actual curative effect is possible. Palliative treatment essential. 80 cases were on the extract for 6 months. Many were in a satisfactory condition on 0.5 g. thrice daily. One or two were getting more than 1 g., the largest dose being 1.375 g. thrice daily. It is evident that the doses of tincture hitherto used by others for the purpose were far too small.—C. Worster-Drought and T. R. Hill, *Lancet*, i/1930, 1225.

45 to 60 minims of B.P. tincture thrice daily increases ability to perform rapid movements. Mental condition improved. May be continued for long period.—E. A. Carmichael, per *Prescriber*, 1929, 224.

If there is interruption of the treatment for even a short time it is necessary to resume with small doses and work up to the maximum (0.25 g. *t.d.s.*).—W. S. Hall, *Lancet*, i/1934, 595.

Marked improvement in the muscular rigidity of post-encephalitic parkinsonism follows the administration of large doses of stramonium combined with pilocarpine to relieve dryness of the mouth. No effect on the tremors. Give 15 m. of Tinct. Stramonii in  $\frac{1}{2}$  oz. of water on waking, after lunch and tea; if the stiffness causes disturbed nights, give another dose at bedtime. All doses of the dilution are increased by 1 drachm on alternate days until the patient complains of dryness of the mouth. Pilocarpine nitrate  $\frac{1}{2}$  gr. is then added to the latest dose of stramonium, and the dose is prescribed in  $\frac{1}{2}$  oz. of water. 1 drachm is again added to each of the doses on alternate days until sufficient relief is obtained or toxic effects (commonly slight paralysis of accommodation) are observed. Finally a prescription is given for the full dose of stramonium (generally at least 60 m.) and pilocarpine nitrate in a single  $\frac{1}{2}$  oz. of water.—A. F. Hurst, *Pharm. J.*, ii/1934, 704.

Pilocarpine is not essential; it may be omitted, and that dose of stramonium alone administered which has been found best suited to the needs of the patient.

—H. Stott, *Indian med. Gaz.*, 1935, 620.

[P1-S1] **Extractum Stramonii (B.P.C.).**

**Dose.**— $\frac{1}{4}$  to 1 grain (0.016 to 0.06 g.).

A soft extract containing 1% of alkaloids.

In spasmodic asthma the extract is found better than the tincture. Sufficient should be given to be slightly toxic. Most patients show toxic effects on taking  $\frac{3}{4}$  grain in 24 hours.

[P1-S1] **Extractum Stramonii (U.S.P. XI).** **Average Dose.**— $\frac{1}{2}$  grain (0.02 g.)

In two forms, pilular and powdered extract, containing 1% of alkaloids

[P1] **Extractum Stramonii Liquidum (B.P. Add. I).**

**Dose.**— $\frac{1}{2}$  to 3 minims (0.03 to 0.2 ml.).

Adjusted to contain 0.25% of alkaloids; 3 minims contains about  $\frac{1}{160}$  grain.

[P1-S1] **Extractum Stramonii Siccum (B.P. Add. I).**

**Dose.**— $\frac{1}{4}$  to 1 grain (0.015 to 0.06 g.). In post-encephalitic and similar conditions, 1 to 8 grains (0.06 to 0.5 g.).

A dry granular extract prepared with alcohol 95%. Contains 1% of alkaloids.

[P1] **Tinctura Stramonii** (*B.P. Add. I*).

*Dose*.—5 to 30 minims (0.3 to 2 ml.); 30 minims contains about  $\frac{1}{16}$  gr. of alkaloids.

Prepared by dilution of the liquid extract 1 in 10 with alcohol 45%. It is approximately half the strength of the *B.P.* '14 tincture.

[P1] **Tinctura Stramonii** (*U.S.P. XI*). *Average dose*.—12 minims (0.75 ml.). 1 in 10 and standardised to contain 0.025% of alkaloids.

[P1] **Unguentum Stramonii** (*B.P.C.*) contains 10% of extract of stramonium.

[P1-S1] **Stramonii Semen** (*B.P.C., P. Helv. V*). *Syn.* THORNAPPLE SEED. The seeds of *Datura Stramonium*, containing an average of 0.2% of alkaloids.

[P1-S1] **Daturæ Folium** (*B.P.C.*). The dried leaves of *Datura Metel* (from India) and of *D. innoxia* (from Mexico and India, and cultivated in England) (*Solanaceæ*). Contains about 0.25 to 0.55% of hyoscyne, with traces only of hyoscyamine and atropine. Used in India for the same purposes as stramonium.

[P1-S1] **Daturæ Semen** (*B.P.C.*). The dried seeds of *D. Metel*, containing about 0.2% of hyoscyne.

[P1] **Tinctura Daturæ Seminis**. *Dose*.—5 to 15 minims (0.3 to 1 ml.). Sedative for asthmatic cough.

[P1-S1] **Daturine**, *dose*.— $\frac{1}{160}$  to  $\frac{1}{100}$  grain (0.0005 to 0.001 g.), is a mixture of alkaloids from *Datura Stramonium* consisting chiefly of hyoscyamine with some atropine. Occurs in white crystals slightly soluble in water, freely soluble in alcohol 90%, chloroform and ether. Occasionally used as a mydriatic.

## STROPHANTHUS

*B.P., F.E. VIII, P. Ital. V, P. Helv. V, etc.*

*Syn.* STROPHANTHI SEMINA.

[P1] "*Strophanthus; glycosides of strophanthus.*"

"Ouabain."

[S1] "*Strophanthus, glycosides of.*"

"Ouabain."

[S6] "*Strophanthus, glycosides of—specify proportion as the amount of Standard Tincture of Strophanthus as defined in the British Pharmacopœia which possesses the same activity as a specified quantity of the preparation when assayed by the method described in the said Pharmacopœia.*"

*Dose*.—No dose is given in *B.P.*

The dried ripe seeds of *Strophanthus Kombé* (*Apocynaceæ*) freed from the awns, of a fawn colour, and covered with hairs. Some foreign pharmacopœias also recognise *S. hispidus* and *S. gratus*.

**Antidotes.** Treat as for poisoning by digitalis, see p. 480.



**Uses.** As a cardiac tonic and diuretic. Resembles digitalis in effects but acts far more promptly. It is stated that the tincture acts in from  $\frac{1}{2}$  to 1 hour, while digitalis tincture takes from 24 to 48 hours, but it is a more dangerous drug to use, since it is easily absorbed. Occasionally of service where digitalis has failed or is not tolerated. Especially valuable in mitral stenosis, but unsuitable in aortic disease. It is non-cumulative and is a better diuretic than digitalis because, while it accelerates the circulation, it does not readily constrict the renal vessels.

[P1-S1] **Extractum Strophanthi** (B.P.C.).

*Dose.*— $\frac{1}{4}$  to 1 grain (0.016 to 0.06 g.).

A dry extract mixed with lactose, so that 2 parts of extract in powder = 1 part of seeds.

[P1-S1] **Tinctura Strophanthi** (B.P.).

*Dose.*—2 to 5 minims (0.12 to 0.3 ml.).

Prepared by percolation, with 70% alcohol, of seeds defatted with light petroleum. The strength is adjusted to be equivalent to that of a 0.42% w/v solution of international standard ouabain or of a 0.33% w/v solution of anhydrous ouabain, the comparison being made by the frog method.

*P. Ital. V, F.E. VIII, P. Belg. IV, Fr. Cx., and I.A.* have 1 in 10. *Fr. Cx.* has max. single dose about 8 minims; max. during 24 hours about 25 minims.

[P1-S1] **Strophanthinum** (B.P., U.S.P. XI). *Syn.* KOMBÉ STROPHANTHIN, K-STROPHANTHIN.

*Dose.*—By intramuscular or intravenous injection,  $\frac{1}{100}$  to  $\frac{1}{80}$  grain (0.00025 to 0.001 g.). *U.S.P. XI* average daily dose, intravenously  $\frac{1}{100}$  grain. It is irritating at the site of injection.

A mixture of glycosides from strophanthus, adjusted by admixture with lactose so as to possess 40% (*U.S.P. XI* 40 to 60%) of the activity of anhydrous ouabain.

**Solubility.** The undiluted mixture of glycosides is moderately soluble in water and in alcohol 90%, less soluble in dehydrated alcohol, sparingly soluble in chloroform, almost insoluble in ether, benzene and light petroleum.

**Contraindicated** where there is a high blood pressure and marked arteriosclerosis, and in those with acute or chronic nephritis or granular kidney.

**Uses.** Strophanthin is usually preferred for intramuscular or intravenous injection to obtain rapid digitalisation in extreme heart failure or when digitalisation by the mouth is impracticable. It is absorbed more rapidly than digitalis and is non-cumulative, but it is an extremely powerful poison and should be used with great caution, especially in cases with myocardial degeneration and coronary sclerosis. If a digitalis preparation has been given during the previous 14 days the dose of strophanthin is best given in fractions several hours apart. Since the effect of a single dose of strophanthin has almost entirely disappeared within 48 hours, the injections may be repeated every other day if required.

There is no degree and no phase of cardiac insufficiency from the beginning of the disease—often difficult to gauge—to the stage of extreme abnormality in the distribution of blood, along with its accompaniments, which does not respond to the intravenous administration of strophanthin. Only the compensated heart on the one hand or the dying heart on the other not yet responds or no longer responds to this treatment. The prognosis of cardiac insufficiency has entirely changed since the possibility has arisen through the use of strophanthin not only of enlarging the field in which treatment with digitalis is indicated, but also of making success in the treatment of certain cases more assured. The heroic treatment of heart failure with calomel and digitalis by mouth is now replaced by one which involves the administration of mersalyl, and so supplements the effect of strophanthin in this disease. The appropriate combination of both remedies, not simultaneously or on the same day even, but one after the other on different days, makes possible the removal of oedema of the severest degree as well as that of very long standing.—A. Fraenkel, *Lancet*, ii/1935, 1104.

Strophanthin is a convenient, effective, cheap and safe drug for rapid reduction of the heart rate when digitalisation by the mouth is impracticable. Reduction in the heart rate is usually obtained in 5 to 15 minutes, and vomiting is rare. Over 200 doses of strophanthin, 1.0 gr. intravenously, were given to 33 patients, of whom 29 had auricular fibrillation. Patients who are febrile require larger doses. The dose of 1.0 gr. can be repeated in one hour if necessary, but should not be repeated until the lowering of the pulse-rate has ceased.—H. E. Rykert and J. H. Hepburn, *Canad. med. Ass. J.*, i/1936, 281.

**ANGINA PECTORIS.** Strophanthin intravenously, given before serious hypertrophic changes in the heart have set in, is of value. The average daily dose is 0.25 mg. and 0.2 mg. is often sufficient. A satisfactory procedure is to give 0.1 to 0.15 mg. on the first day, 0.2 mg. on the second day, and 0.3 mg. on the third day, and to continue a course of injections for four to six weeks. High dosage, sometimes as much as 1 mg. in 24 hours, distributed over four to six injections, is particularly desirable in cases of recent infarct of the myocardium. A follow-up study of 32 patients treated on these lines showed that 26 had been completely or almost completely relieved, and that some had continued to remain fit in spite of heavy physical work.—H. Plugge and E. Birk, *Dtsch. med. Wschr.*, i/1937, 427.

[P1-S1] **Kombetin** (Boehringer, Mannheim; Coates & Cooper, London). Glycoside from *Strophanthus Kombé*. Ampoules of 1 ml. = 0.0005 g. or 0.00025 g. Dose.—Initially 0.00025 g. intravenously; 0.0005 g. as average dose in 24 hours.

[P1-S1] **Strophanthone Dilute** (Parke, Davis, London). Preparation of *Strophanthus Kombé* seed in ampoules for hypodermic or intravenous administration. 1 ml. represents the activity of 0.12 ml. of tincture of *strophanthus*, B.P.

Dose.—Hypodermically, 1 ml. initially, subsequently as required. Intravenously, 0.5 ml.

[P1-S1] **Strophosid** (Sandoz, London). A new glycoside, K-strophanthosid, isolated from the seeds of *Strophanthus Kombé* in a crystalline state. Supplied in ampoules; 1 ml. = 0.0005 g. of K-strophanthosid. Dose.—0.4 to 1 ml. intravenously. In grave acute cardiac weakness, in cardiac weakness with a slow pulse, in overstrain of the heart, in the end stages of decompensation in valvular insufficiency and hypertonia, in cardiac weakness without hypertrophy and in some forms of myocardial degeneration, e.g., in diphtheria.

[P1-S1] **Ouabainum** (Fr. Cx.). Syn. G-STROPHANTHIN, STROPHANTHINUM (P.G. VI, P. Dan.).  $C_{30}H_{46}O_{12} \cdot 9H_2O = 760.5$ .

Dose.— $\frac{1}{200}$  to  $\frac{1}{100}$  grain (0.00025 to 0.001 g.), by injection. P.G. VI max. single dose  $\frac{1}{100}$  grain; max. daily dose  $\frac{1}{20}$  grain.

Obtained from *S. gratus* seeds, also present in wood of *Acokanthera Schimperi* (Apocynaceæ). Is about twice as toxic as K-strophanthin, and is used as an international standard for control of the standard preparation of strophanthin which is used for the biological assay of strophanthin and *strophanthus* preparations.

[P1-S1] **Ouabaine** Arnaud (Laboratory Nativelle, London). Crystalline ouabaine obtained from *S. gratus*. Supplied in tablets (5 mg.); 2% solution for oral use (50 drops = 20 mg.); ampoules for intravenous injection (1 ml. = 0.25 mg.); ampoules for intramuscular injection (2 ml. = 0.5 mg.).

[P1-81] **Natibaine** (*Laboratory Nativelle, London*). 1 in 1000 glycerin alcohol solution of  $\frac{1}{2}$  Nativelle's Digitaline and  $\frac{1}{2}$  Ouabaine Arnaud, 15 drops containing  $\frac{1}{320}$  gr. of the former, and  $\frac{1}{320}$  gr. of the latter. *Dose*.—15 to 50 drops (according to the degree of cardiac insufficiency) for the first five of each 10 or 15 days, given in a small quantity of water on an empty stomach before rising, or at bedtime; when the daily dose is 30 drops or more it should be divided into two parts. The combination provides both a rapid and a prolonged action in myocarditis with arrhythmia and ventricular dilatation, in complete arrhythmia and arterial hypertension with tendency to tachycardia.

## STRYCHNINA

*B.P.C., Fr. Cx., F.E. VIII, etc.*



[P1] "*Alkaloids, the following; their salts, simple or complex:—Strychnine.*"

[81] "*Alkaloids, the following; their salts, simple or complex:—Strychnine except substances containing less than 0.2 per cent. of strychnine.*"

*Rule 15 of the Poisons Rules, 1935, prohibits the sale or supply of strychnine (or its salts) except in certain circumstances, see page 1007.*

*Dose*.— $\frac{1}{32}$  to  $\frac{1}{8}$  grain (0.002 to 0.008 g.). *Fr. Cx.* has max. single dose  $\frac{1}{16}$  grain; max. during 24 hours  $\frac{1}{4}$  grain approx.

The alkaloid obtained from *nux vomica*, St. Ignatius' beans (*q.v.*), and the seeds of other species of *Strychnos*. In characteristic colourless crystals.

**Soluble** 1 in 7000 of water, about 1 in 400 of alcohol 60%, 1 in 150 of alcohol 90%, 1 in 350 of dehydrated alcohol, 1 in 6 of chloroform, nearly insoluble in ether.

*Precipitation by Iodides.* As long as the maximum dose of either strychnine or an iodide is prescribed in half a fluid ounce, the precipitation of strychnine hydriodide is not likely to occur. It will, however, occur if maximum doses of both are present.—*Pharm. J.*, i/1939, 190.

**Antidotes.** If patient is seen at once, empty stomach by emetics or stomach tube, but if tetanic symptoms have already set in, first give chloroform as anæsthetic and then use the stomach tube with a solution of 60 gr. of potassium permanganate in 2 gallons of water. Give medicinal charcoal, stirred up in water, freely.

(Some authorities say that emetics and the stomach tube must not be used or fatal convulsions may be caused. Give potassium permanganate in 10 gr. doses, or medicinal charcoal.)

Keep patient lying down and quiet, fully under chloroform if necessary. If convulsions persist, give potassium bromide 4 dr., and chloral hydrate 30 gr., repeating every hour if necessary. Soluble barbitone, soluble phenobarbitone or sodium Amytal intravenously considered of value. Saline with dextrose infusion. Artificial respiration and inhalations of oxygen with 7% carbon dioxide.

6 gr. of strychnine hydrochloride taken for suicidal purposes; patient given 30 gr. of zinc sulphate within 20 minutes, chloroform anaesthesia and  $\frac{1}{4}$  gr. morphine hypodermically. He became cyanosed, was given amyl nitrite, gastric lavage with potassium permanganate solution, some left in stomach. Later morphine and atropine given, chloral hydrate and potassium bromide by rectum, more morphine and atropine. Anaesthesia maintained, amyl nitrite repeated, also chloral and bromide. Oxygen with carbon dioxide administered for  $\frac{1}{2}$  hour. Spasms diminished, cyanosis lessened, respiration improved, patient drank water, slept, vomited and was discharged well next day. Severe asphyxia was not relieved by chloroform anaesthesia with morphine until amyl nitrite also given.—*Brit. med. J.*, i/1936, 363.

Poisoning in U.S.A. caused 546 deaths from 1926 to 1928, compared with 11 for England and Wales for 1930 to 1931. One-third of the accidental poison deaths occur in children under 5 years of age, due to the popularity of "tonic" tablets containing strychnine.—*Brit. med. J.*, ii/1932, 159.

Recovery of a man aged 60 after taking 15 g. in water. An hour and a half later he was given 0.5 g. of sodium Amytal intravenously and was relaxed and sound asleep within 15 minutes.—*R. E. Priest, J. Amer. med. Ass.*, i/1938, 1440.

**Uses.** Given orally, strychnine acts as a bitter stomachic and as a stimulant to the central nervous system, and is of value in dyspepsia and chronic gastritis and as a general tonic in anaemia and convalescence. As a stimulant to the central nervous system it has been widely used in almost every form of paralysis, and as long as distinct anatomical lesions of the central nervous axis are absent it may be of benefit, but when the paralysis is due to an inflammatory process it is better avoided. As a circulatory stimulant and vaso-constrictor it is of value in a wide variety of conditions, such as surgical shock, cardiac failure, collapse from hæmorrhage, poisoning by depressants, such as ether or chloroform, and in the acute stage of severe infectious diseases, such as diphtheria; in these conditions it is given in doses up to  $\frac{1}{16}$  gr. by hypodermic injection. As a respiratory stimulant it may be used by the mouth, in combination with expectorants, in chronic bronchitis or emphysema, or it may be given by injection in frequently repeated doses in severe bronchitis and pneumonia. Its stimulant action on the respiratory centre is especially valuable in narcotic poisoning, e.g., by opium or chloral; in barbiturate poisoning it is given in doses as high as  $\frac{1}{4}$  gr. without toxic effect. Strychnine has also been found useful in toxic amblyopia (especially that due to nicotine poisoning) and amaurosis.

**DIPHTHERIA.** There is still a small group of cases in which serum, though administered early and in sufficient dosage, appears to fail. All patients with really severe diphtheria should be given strychnine in large doses, i.e., subcutaneously to the amount of 1 mg. per kg. of bodyweight in every 24 hours. For practical purposes the total amount required on this formula is divided by 8 to give the dose administered every three hours, which is held to be the best interval. As a rule the maximum dose is not given at once; at first it is halved and the maximum is slowly reached in three or four days. In really desperate cases doses even as high as 1.5 to 2 mg. per kg. have been given. The treatment is continued for a fortnight and signs of intolerance must be carefully looked for. Tolerance is actually much greater than has been previously imagined, and is fortunately greatest in children and in states of collapse. As the earlier signs of intolerance (headache and vertigo) are subjective, small children need special attention. If increased reflexes and a positive Chvostek appear, the treatment must be temporarily abandoned, but may be resumed later. In the presence of such signs of poisoning as clonic contractions or strychnine tetany, chloroform must be administered at once to prevent asphyxia.—*Faisseau et al., Fr. méd.*, 1936, 1241.

**[P1-S1] Ferri et Strychninæ Citras (B.P.C.).**

*Dose.*—1 to 3 grains (0.06 to 0.2 g.).

In deliquescent green scales, freely soluble in cold water. It contains 1% of strychnine, and about 13% of Fe.

**[P1-S1] Ferri, Quininæ et Strychninæ Citras (B.P.C.).**

*Dose.*—2 to 5 grains (0.12 to 0.3 g.).

Similar to the former, with about 15% of quinine. In deliquescent scales, soluble 1 in 2 of water.

**[P1-S1] Strychninæ Arsenas.  $C_{21}H_{22}O_2N_2, H_3AsO_4, \frac{1}{2}H_2O = 485.1$ .**

*Dose.*— $\frac{1}{10}$  to  $\frac{1}{5}$  grain (0.001 to 0.004 g.).

In small white acicular crystals containing 68.7% of strychnine, soluble 1 in 14 of water. Has been used in phthisis by hypodermic injection.

**[P1-S1] Strychninæ Hydrochloridum (B.P.).**

$C_{21}H_{22}O_2N_2, HCl, 2H_2O = 406.7$ .

*Dose.*— $\frac{3}{32}$  to  $\frac{1}{8}$  grain (0.002 to 0.008 g.).

Small trimetric prisms, soluble 1 in about 40 of water, 1 in about 80 of alcohol 90%; insoluble in ether.

A 1% w/v solution is strongly hypotonic; 0.079 g. of sodium chloride or 0.442 g. dextrose to every 10 ml. renders it isotonic.

**[P1-S1] Injectio Strychninæ (B.P.C.).**

*Dose.*—5 to 10 minims (0.3 to 0.6 ml.), by hypodermic injection.

Contains 0.75% w/v of strychnine hydrochloride; 10 minims contains about  $\frac{1}{15}$  grain.

**[P1-S1] Liquor Strychninæ Hydrochloridi (B.P.).**

*Dose.*—3 to 12 minims (0.2 to 0.8 ml.); 12 minims contains about  $\frac{1}{8}$  gr. of strychnine hydrochloride.

Strychnine hydrochloride 1, alcohol (90%) 25, water to 100.

**Incompatible** with alkalis, e.g., sodium bicarbonate, sal volatile, bromides and iodides.

It is safer to prescribe tincture of nux vomica in preference to solution of strychnine hydrochloride when there is danger of incompatibility.

**[P1] Mist. Acid. c. Strych. (N.I.F.).** Dilute hydrochloric acid 10 m., solution of strychnine hydrochloride 3 m., chloroform water to  $\frac{1}{2}$  oz.

**[P1-S1] Strychninæ Nitras (B.P.C., U.S.P. XI, P.G. VI, P. Belg. IV, P. Hung., P. Helv. V, P. Dan., P. Ital. V, F.E. VIII).**

$C_{21}H_{22}O_2N_2, HNO_3 = 397.2$ .

*Dose.*— $\frac{3}{32}$  to  $\frac{1}{8}$  grain (0.002 to 0.008 g.). *P. Helv. V* and *P. Hung.* give max. single dose  $\frac{1}{8}$  grain; max. in 24 hours  $\frac{1}{4}$  grain. *P.G. VI* gives half these amounts; *F.E. VIII*  $\frac{1}{80}$  and  $\frac{1}{12}$  grain respectively. *U.S.P. XI* average dose  $\frac{3}{32}$  grain.

Colourless needles, soluble 1 in 60 of water (1 in 45 at 25°—*U.S.P. XI*), 1 in 120 of alcohol 90%.

Injections varying from  $\frac{1}{15}$  to 1 gr. hypodermically have been employed with success in the treatment of snake bite.

**[P1-S1] Injectio Strychninæ, Arseni Iodidi et Quininæ.** Strychnine nitrate 1 gr., arsenic triiodide 2 gr., quinine lactate 1 dr., distilled water to 3 oz.

*Dose.*—Up to 1 drachm hypodermically for adults.

Specific to reduce temperature in influenza attacks and almost any grave affection. Also prophylactic, e.g., in malaria.

[P1-81] **Strychninæ Sulphas** (B.P.C., U.S.P. XI, Fr. Cx., F.E. VIII, P. Ital. V).  $(C_{21}H_{22}O_2N_2)_2 \cdot H_2SO_4 \cdot 5H_2O = 856.5$ .

Dose.— $\frac{1}{32}$  to  $\frac{1}{8}$  grain (0.002 to 0.008 g.). Fr. Cx. has max. single dose  $\frac{1}{10}$  grain; max. during 24 hours  $\frac{1}{4}$  grain approx. F.E. VIII  $\frac{1}{60}$  and  $\frac{1}{12}$  grain respectively. U.S.P. XI average dose  $\frac{1}{30}$  grain.

The neutral salt is in prismatic crystals, **soluble** 1 in 62 of water and 1 in 135 of alcohol 90%. M. p. 200°. It contains  $5\frac{1}{2}H_2O$ , i.e., there is usually a loss on drying of 11.44% approx.

[P1-81] Granules de Sulphate de Strychnine (Fr. Cx.) contain 1 mg. in each granule.

[P1-81] **Strychninæ Sulphas Acidus**. Syn. HULLE'S SOLUBLE STRYCHNINE.  $C_{21}H_{22}O_2N_2 \cdot H_2SO_4 \cdot 2H_2O = 468.3$ .

Dose.— $\frac{1}{40}$  to  $\frac{1}{10}$  grain (0.001 to 0.004 g.).

In white silky acicular crystals with a slightly acid reaction, soluble 1 in 42 of water.

[P1-81] **Strychninæ Valerianas**.

A non-crystallisable salt supplied in aqueous solution equivalent to 25% of the base. Dose.— $\frac{1}{25}$  minim to  $\frac{1}{10}$  minim ( $=\frac{1}{125}$  to  $\frac{1}{30}$  grain of the base). A useful nerve tonic.

**Brucine**.  $C_{23}H_{26}O_4N_2 \cdot 4H_2O = 466.3$ .

[P1] "Alkaloids, the following; their salts, simple or complex:—**Brucine**."

[81] "Alkaloids, the following; their salts, simple or complex:—**Brucine** except substances containing less than 0.2 per cent. of brucine."

Dose.— $\frac{1}{32}$  to  $\frac{1}{4}$  grain. An alkaloid from *Strychnos Nux Vomica* seeds—small white acicular crystals, with bitter taste.

Very **soluble** in alcohol and chloroform. Its salts are soluble in water. It is said to possess only  $\frac{1}{12}$  of the physiological power of strychnine.

[P1-81] **Curara** (B.P.C.). Syn. CURARE, OURARI, URARI, WOURARA, WOURALI.

[P1] "Alkaloids, the following; their salts, simple or complex:—**Curarine**."

[81] "Alkaloids, the following; their salts, simple or complex:—**Curarine**."

Dose.— $\frac{1}{32}$  to  $\frac{1}{4}$  grain (0.003 to 0.03 g.) subcutaneously.

Curare, the South American Indian arrow poison, is an extract derived from the bark of various species of South American *Strychnos*. Commercial "calabash" curare is derived from *S. toxifera*; "pot" curare from *S. Castelnaei* together with *Cocculus toxiferus* (Menispermaceæ), while "tube" curare is from unknown plants. It is a blackish-brown dry extract, with bitter taste; contains some resin, but is nearly all soluble in water.

**Uses.** The chief effect of curare is to paralyse the voluntary movement by blocking the passage of impulses from the peripheral nerves to the muscles. The respiratory muscles are last affected, and death takes place from asphyxia. Curare has been used in the treatment of tetanus in conjunction with antitoxin, and

paraldehyde or bromethol *per rectum*. It is given subcutaneously (it is inactive orally) in a dose of 0.03 g., usually repeated at six-hourly intervals. Its use is best reserved for severe cases.

Given intramuscularly or intravenously in doses between 10 and 40 mg., which have to be carefully adjusted to the individual patient, it quickly relaxes the hypertonic muscles in spastic-paralytic and dystonic conditions. The effect is rapid, but soon starts to diminish, though it may be noticeable after two days. For therapeutic purposes the drug has to be given at least three times a week. Administration may be accompanied by transient unpleasant effects, such as giddiness, diplopia and mild confusion. For the maximum benefit to be obtained, simple orthopedic operations may be required, and continuous training of the muscles should run parallel with the administration of the drug.—M. S. Burman, *Arch. Neurol. Psychiat.*, 1939, 41, 307.

[P1-81] **Curarine.**  $C_{19}H_{26}ON_2 = 298.2$ .

The active principle of gourd curare, in yellowish powder soluble in water and in alcohol. This curare also contains curine, identical with beberine. Bamboo (tube) curare and pot curare contain allied alkaloids.

A case of tetanus successfully treated by curarine in conjunction with anti-tetanic serum intravenously. A sterile solution of curarine hydrochloride (free from curine) containing 1 mg. in 1 ml. was prepared freshly every few days and given subcutaneously; initial dose 0.1 mg. repeated 4-hourly, the size of dose and frequency of administration being slowly increased daily until 8 doses of 0.5 mg. were being given in 24 hours. In all, 48.1 mg. of curarine were given in 20 days.—J. S. Mitchell, *Lancet*, i/1935, 262.

Curarine treatment of tetanus should still be reserved for cases which are already very severe or in which, by the accepted criteria, the prognosis is very grave. The best method of giving it is by the intravenous drip, using curarine chloride in solution, 100 mg. of the solid to a pint of saline or glucose saline, and adjusting the inflow so as to deliver 0.25 mg. per kg. of bodyweight per hour to the patient, arranged so as to be equivalent to about 30 drops per minute in the dripper. A pint of solution lasts about 6½ hours. At first the solution is run in at 6 times its maintenance rate, so that 0.25 mg. per kg. is delivered in about 10 minutes; this should be sufficient for curarisation. During this period and for the first hour following administration at maintenance rate its effects should be closely watched, since a real danger of curarine treatment is the sudden onset of bronchial spasm. Animal experiments justify the administration of atropine  $\frac{1}{100}$  to  $\frac{1}{20}$  gr. hypodermically before and at 4-hour intervals during the period of curarisation, and a full dose of adrenaline if the spasm occurs. Curarine in its present form is unsuitable for treatment of cases of chronic rigidity, and is given in tetanus only as a means of removing muscular spasm—antitoxin is required as urgently as with any other treatment.—R. West, *Lancet*, i/1936, 12.

**Erythrina.** An alcoholic extract of the seeds of *Erythrina americana* (Leguminosæ) possesses a typical curare-action in amphibia, mammals and birds. The *Erythrina americana* is a shrub or tree, indigenous to Mexico and Vera Cruz; it bears brilliant red flowers and a many-seeded fruit with scarlet seeds. It was used by the Aztec Indians as a purgative, diuretic, sudorific and hypnotic. Erythrina is as potent as curare, but the duration of paralysis can be more easily controlled by carefully grading the dose. It is effective by hypodermic, intramuscular and intravenous injection, but not by gastric administration. It is a promising, comparatively easily available, and practical substitute for curare.—A. J. Lehman, *J. Pharmacol.*, 1937, 60, 69.

**Ibogaine.**  $C_{17}H_{15}O_2N_2 = 306.6$ . An alkaloid obtained from the Iboga (*syn.* aboua, obouete, or liboka) *Tabernanthe Iboga* (Acanthaceæ), a plant growing in West Africa, particularly the Congo. Said to have aphrodisiac and sustaining powers. Too large a dose may produce tetanus and convulsions. The plant has been tried in sleeping sickness. The base is soluble 1 in 28 of alcohol 95%, insoluble in water. It has been given in dose 0.005 g. ( $\frac{1}{20}$  grain). **Ibogaine Hydrochloride** has been given in influenza, and in angina pectoris and other heart affections.

**Muira-Puama.** This drug, which comes from Brazil, is said to be derived from *Liriosma ovata* (Olacaceæ). It has an irritating action and tonic aphrodisiacal properties. Used in nervous disorders.

**Picrotoxinum** (B.P.C.).  $C_{30}H_{34}O_{13} = 602.3$ .

[P1] "*Picrotoxin.*"

[S1] "*Picrotoxin.*"

**Dose.**— $\frac{1}{100}$  to  $\frac{1}{5}$  grain (0.0006 to 0.0025 g.).

Colourless odourless crystals or microcrystalline powder extracted from cocculus indicus. M.p. about 200°.

**Soluble** 1 in 334 of water, 1 in 35 of boiling water, 1 in 13.5 of alcohol 90%, 1 in 10 of solution of potassium hydroxide, also soluble in organic solvents.

**Antidotes.** Empty stomach by emetic or stomach tube. Give medicinal charcoal stirred up in water. For convulsions, give potassium bromide 2 dr. and chloral hydrate 20 gr., repeated if necessary. Soluble barbitone, soluble phenobarbitone, or sodium Amytal intravenously. Keep patient lying down and warm.

**Uses.** It is a powerful convulsive poison, differing from strychnine in that it acts mainly on the medulla. Gives good results in checking night-sweats (does not, like atropine, cause dryness of the throat), also employed in epilepsy and chronic alcoholism: overdoses cause stupor, delirium and convulsions. It increases the secretion of the mucous and sweat glands. It may be given in pills, to be taken for 2 or 3 nights successively. The drug is slightly cumulative, and may thus be temporarily stopped with effects persisting. A pill of picrotoxin  $\frac{1}{80}$  gr., atropine  $\frac{1}{80}$  gr., with agaricin  $\frac{1}{4}$  gr., is said to act even better than picrotoxin alone.

Its convulsant action is employed in the treatment of barbiturate poisoning, for which purpose a dose of from 1 to 10 mg. is given intramuscularly or intravenously; owing to its rapid excretion the injections need to be repeated at frequent intervals. It is also used similarly to leptazol in the convulsion treatment of schizophrenia, and is said to give rise to less unpleasant effects than other convulsant drugs.

**BARBITURATE POISONING.** To counteract the coma give 5 mg. of picrotoxin intravenously in 0.2% aqueous or normal saline solution. If no awakening effect is produced in 20 to 30 minutes give another 5 mg., followed, if necessary, after another 20 minutes by a further dose of 10 mg. Discontinue when twitches occur until the patient again becomes lethargic. Continue with smaller doses, 3 to 5 mg., until the patient emerges from coma. As much as 150 to 200 mg. over a period of 48 hours have been given.—W. S. Murphy *et al.*, *J. Lab. clin. Med.*, 1937, 22, 350. See also J. L. Lovibond, *Lancet*, ii/1939, 561.

Of four cases of barbiturate poisoning treated with picrotoxin one died and three recovered. One patient recovered after receiving 671 mg. of picrotoxin. The picrotoxin is best given intravenously in fractional doses (from 3 to 12 mg.), the size and interval depending on the degree of depression and the response of the patient. In the event of an accidental overdose of picrotoxin, resulting in convulsions which do not subside within one or two minutes, a slow intravenous injection of a suitable barbiturate will control them immediately, and such a barbiturate should always be on hand when picrotoxin is administered.—R. Kohn *et al.*, *J. Amer. med. Ass.*, ii/1938, 387.

In six cases of barbiturate poisoning treated by picrotoxin, a safe convenient method for the administration of picrotoxin was used. Effective treatment of



barbiturate poisoning emphasised the following procedure: (a) gastric lavage and purgation, (b) continuous oxygen, (c) the administration of picrotoxin intravenously (1 in 1000 solution at the rate of 1 ml. per minute) until the return of pupillary and corneal reflexes, (d) diuresis by parenteral fluids and intravenous sucrose, and (e) the administration of dextrose to prevent acidosis.—W. J. Bleckivenn and M. G. Masten, *J. Amer. med. Ass.*, ii/1938, 504.

The experimental basis for its efficacy in barbiturate poisoning is fairly strong. In addition to the customary supportive measures, the general practice is to use doses of from 1 to 10 mg. of picrotoxin intramuscularly or intravenously at intervals of 30 minutes, until signs of stimulation occur, and to maintain this state by appropriate repetition of similar or smaller doses as long as indicated by the state of depression.—Report of the Council of Pharmacy and Chemistry, *J. Amer. med. Ass.*, i/1939, 431.

Animal experiments show that picrotoxin rapidly disappears from the blood. There is a rapid fall in blood picrotoxin occurring immediately after injections and levelling off after about 20 minutes. This is probably due to the taking up of picrotoxin by the tissues. At the end of two hours the quantities of picrotoxin were practically negligible. This means that when picrotoxin is used in the treatment of barbiturate poisoning, frequent administration is necessary in order to maintain effective concentrations.—D. M. Duff and J. M. Dille, *J. Pharmacol.*, 1939, 67, 353.

Intravenous injections of 10 ml. of a 1 in 1000 solution gave recovery in four out of 5 cases of collapse due to barbiturates.—S. W. Gillman, *Lancet*, i/1940, 598.

**SCHIZOPHRENIA.** Out of a series of 38 cases, 18 either had a full recovery or were socially recovered. The drug was injected intravenously in dosage determined for each individual patient; the convulsions produced were not preceded by the interval of acute terror often noted with other convulsant drugs.—A. A. Low et al., per *J. Amer. pharm. Ass., pharm. Abstr.*, 1940, 40.

Picrotoxin is very much slower in action and is almost free from the unpleasantness sometimes associated with Cardiazol and Triazol, and it would seem the most suitable convulsant yet used in the shock treatment of certain mental illnesses. It was administered by intravenous injection in 22 cases, the initial dose being 4 ml. of a 0.3% aqueous solution, increased when necessary by increments of 0.5 ml., the total number of injections being gauged by the clinical response.—J. S. Horsley, *Med. Pr.*, i/1940, 70.

[P1-S1] **Cocculus Indicus** (B.P.C.). *Syn.* LEVANT BERRIES.

The fruit of *Anamirta paniculata* (Menispermaceae), containing 1.0 to 1.5% of picrotoxin. Has been used as an ointment for pediculi (1 in 60) also as tincture (1 in 10) and liquid extract (1 in 1).

**Yohimba** (B.P.C.).

[P1] "Alkaloids, the following; their salts, simple or complex:—Yohimba, alkaloids of."

[S1] "Alkaloids, the following; their salts, simple or complex:—Yohimba, alkaloids of."

[S6] "Alkaloids—Yohimba, alkaloids of—specify proportion as the proportion of any one alkaloid of yohimba that the preparation would be calculated to contain on the assumption that all the alkaloids of yohimba in the preparation were that alkaloid."

The bark of *Pausinystalia yohimba* (Rubiaceae), containing 0.3 to 1.5% of alkaloids, chiefly yohimbine.

[P1-S1] **Yohimbinae Hydrochloridum** (B.P.C., *Fr. Cx.*, *P. Helv.* V).  $C_{21}H_{26}O_3N_2 \cdot HCl = 390.7$ .

*Dose.*— $\frac{1}{15}$  grain to  $\frac{1}{2}$  grain (0.003 to 0.008 g.), in pills or by hypodermic injection. *Fr. Cx.* has *max. single dose* about  $\frac{1}{2}$  grain; *max. in 24 hours*  $\frac{1}{2}$  grain.

White odourless crystalline powder with bitter taste. M.p. about 300°.

**Soluble** 1 in 100 of water, more soluble in hot water and in alcohol 90%.

**Uses.** Aphrodisiac, increasing the pelvic reflexes. A few drops of a solution  $\frac{1}{2}$  to 1% strength act as an anæsthetic when applied to the cornea.

[P1-S1] **Yohimbina.** *Syn. and Prop. Name.* CORYNINA, APHRODINE (C. Zimmermann, London). In white crystals soluble in organic solvents; m.p. 234°.

[P1-S1] **Juvenin** (Bayer Products, London). Yohimbine methylarsinate and strychnine methylarsinate. *Dose.*—1 tablet (0.1 g.) thrice daily or 1 ml. subcutaneously every second day. For sexual neurasthenia.

[P1-S1] **Menolysin** (Coates & Cooper, London). Yohimbine hydrochloride in tablets (0.005 g.) and ampoules for subcutaneous injection (0.05 g. in 1 ml.). In dysmenorrhœa and amenorrhœa.

[P1-S1] **Tonicamps** (Paines & Byrne, London). Ampoules of 1 ml. containing strychnine and yohimbine monomethylarsenate. Asthenia and sexual impotence.

## SULPHANILAMIDUM

(with SULPHAPYRIDINE and SULPHATHIAZOLE)



*Syn. and Prop. Names.* SULFANILAMIDUM (U.S.P. XI Supp. II), SULPHONAMIDUM, SULPHONAMIDUM-P, AMBESID (Richter, London), COLSULANYDE (Crookes Laboratories), P.A.B.S. (Hewlett & Sons, London), PRONTOSIL ALBUM (Bayer Products, London), RUBIAZOL-A (Roussel Laboratories, London), STREPTOCIDE (Evans, Sons, Lescher & Webb, Liverpool).

[P1], [S1] and [S4] "*Para-aminobenzenesulphonamide; its salts; derivatives of para-aminobenzenesulphonamide having any of the hydrogen atoms of the para-amino group or of the sulphonamide group substituted by another radical; their salts.*"

*Dose.*—In cases of serious infection in adults 15 grains (1 g.) every four hours for 48 hours followed by from  $7\frac{1}{2}$  to 10 grains (0.5 to 0.66 g.) every four hours thereafter. It is usually advisable to continue dosage for a few days after clinical recovery in order to avoid a relapse. Infants will tolerate from one-third to one-half the adult dose, and children from one half to three quarters. U.S.P. XI Supp. II has average daily dose 45 grains (3 g.). (For further details as to dosage and technique of administration see **USES**).

Dosage of sulphanilamide derivatives for children. A method of estimating the concentration in the blood and a table of suggested dosages at various ages.—M. Hynes, *Lancet*, i/1940, 261.

Sulphanilamide is *p*-aminobenzenesulphonamide or *p*-aminophenylsulphonamide, prepared by the action of ammonia on the chlorsulphone obtained by treating acetanilide with chlorsulphonic acid, followed by hydrolysis. It occurs as a white, crystalline powder, odourless, but with a slightly bitter taste. M.p. 165.5°.

**Introduction.** Sulphanilamide was first synthesised by Gelmo in 1909, but it was not until 1935 that Domagk showed that an azo dye containing a sulphanilamide nucleus prevented the development of streptococcal septicaemia in mice. This substance, originally marketed under the trade name Prontosil, but later called Prontosil Rubrum, was highly efficacious in experimental and clinical infections, but possessed the disadvantages of low solubility with some toxicity. Subsequently it was shown that it was the sulphanilamide nucleus that was responsible for the streptococcidal activity of Prontosil Rubrum, and that it was less toxic than the azo dye. At first sulphanilamide was considered specific for hæmolytic streptococci, but later work has shown that it is of value in the treatment of a number of other infections including meningococcal, gonococcal and urinary tract (*B. coli*) infections.

**Soluble** 1 in 125 of cold water, but very soluble in hot water; also soluble 1 in 37 of alcohol 95%, 1 in 5 of acetone, and in glycerin and hydrochloric acid; slightly soluble in benzene, chloroform and ether.

Preparation for injection of aqueous solutions of *p*-aminobenzenesulphonamide may be accomplished by using solutions of readily soluble quinine salts, such as the glutamate, or of quinine salts containing known dissolution promoters for quinine, such as urethane, as solvents. This process is patented.—per *Brit. chem. Abstr. (B)*, 1939, 884.

**Toxic Effects.** Sulphanilamide, in common with all the other members of the sulphonamide group, is liable to give rise to unpleasant reactions. These vary in their severity according to the dosage, length of administration, and the idiosyncrasy of the patient. The majority of patients during administration suffer from mild toxic reactions, such as malaise, headache, nausea, vomiting, abdominal pains, depression, tinnitus, loss of taste, dizziness, and disturbances of vision. These reactions are more likely to occur if the patient is ambulatory, and patients receiving the drug should be warned against driving motor-cars, piloting aeroplanes, or doing heavy or dangerous work during treatment. Practically all patients develop some degree of cyanosis, though this may be confined in most cases to the lips, ears, and nail beds. Though somewhat alarming, it is not in itself a serious complication unless it is of a progressive character and is accompanied by other symptoms, such as sickness, shallow breathing and mental distress, and it may be successfully controlled in the majority of cases by the administration of methylene blue in pill form, in a dose of 1 or 2 gr. three times daily. The condition is thought to be due to methæmoglobinæmia or sulphæmoglobinæmia, though both of these conditions have been detected spectroscopically in patients showing no clinical cyanosis. A rise of temperature due to the use of the drug, and occurring between the fifth and tenth day of treatment, is a not uncommon toxic reaction, and skin rashes of markedly varying types are also met with fairly frequently.

Many of these minor reactions are dependent for their occurrence, or their severity, on the patient's idiosyncrasy. Thus, certain susceptible individuals may develop a cutaneous sensitivity, associated with porphyrinuria, when exposed to sunlight during sulphanilamide therapy, and wherever possible it is advisable for all patients receiving sulphanilamide to keep out of the sun and to avoid ultra-violet irradiation. Acidosis may also occur in certain individuals, though the routine administration of sodium bicarbonate generally prevents this complication. The concurrent use of ascorbic acid, 0.5 g. daily by injection, or of nicotinic acid, 50 mg. by the mouth three times daily, reduces the incidence of unpleasant symptoms and clears up the mental apathy so often present during treatment.

In addition to these minor toxic effects, sulphanilamide therapy may give rise on occasion to more severe complications. These are, fortunately, comparatively rare, and are usually (though not always) the result of large dosage or prolonged administration. Thus, acute hæmolytic anæmia may occur during the third to fifth day of treatment, and granulocytopenia may occur at any time during the course of administration. Cases of toxic hepatitis have also been recorded with some fatalities.

It is of the utmost importance, in the case of prolonged treatment, to keep a careful watch on the blood picture; patients who have had treatment with the drug for ten days should have white cell counts done every three or four days, since there are no other clinical signs of granulocytopenia, apart from a deterioration of the general condition and continued fever.

In order to avoid the onset of sulphæmoglobinæmia, the use of sulphur-containing foods, and of purgatives, particularly saline purgatives, during sulphanilamide treatment should be avoided, though liquid paraffin is permissible. Similarly, the use of phenacetin, amidopyrine, gold salts, and organic arsenical preparations, should also be avoided.

As sulphanilamide is excreted more slowly in patients with impaired renal function, it should be given with caution in all cases of renal insufficiency.

#### Clinical References to Toxic Effects.

**ANÆMIA.** Anæmia and agranulocytosis during sulphanilamide therapy.—G. H. Jennings and G. Southwell-Sander, *Lancet*, ii/1937, 898.

Three cases of acute hæmolytic anæmia developed during treatment of infections with large doses of sulphonamide. Two patients did not react to small doses of the drug given after they had recovered; the anæmia was therefore different from that resulting from idiosyncrasy and resembled that due to phenylhydrazine. In each case recovery was rapid after the medication was stopped and transfusions of citrated blood had been given.—A. M. Harvey and C. A. Janeway, *J. Amer. med. Ass.*, ii/1937, 12.

A case of anæmia with acute hæmolysis and hæmoglobinuria, following the use of sulphanilamide in a child of one year.—S. E. Kohn, *J. Amer. med. Ass.*, ii/1937, 1005.

Twenty-one cases of acute anæmia occurred in a series of 522 patients treated with the drug, the incidence being higher in children than adults. The earliest signs of the anæmia appeared between 24 and 72 hours after the onset of treatment, the maximum anæmia occurring usually on the fifth day. There were no

deaths. The anæmia is treated by the immediate withdrawal of sulphanilamide, the forcing of fluids, and blood transfusions. It is important that the hæmoglobin should be watched carefully during the first week of sulphanilamide therapy.—W. B. Wood, *J. Amer. med. Ass.*, ii/1938, 1916.

**CYANOSIS.** The commonest toxic effect of the sulphonamide compounds, apart from such minor ones as nausea and depression, is cyanosis. The mechanism by which this cyanosis is produced is not fully understood, but methæmoglobinæmia is regarded as one of the causes. Methylene blue has been shown greatly to accelerate the reversion of methæmoglobin to hæmoglobin in poisoning by various aniline derivatives, and its effect in methæmoglobinæmia due to sulphanilamide is dramatic, the cyanosis disappearing within half an hour when a dose of 1 to 2 mg. of the dye per kilo bodyweight is given intravenously. Though a single dose gives only temporary relief, the methæmoglobin level can be kept low by continuing administration of the dye by the mouth, or prevented from ever rising unduly if methylene blue is given together with sulphanilamide from the start of treatment. The dye itself is believed to be harmless in the doses required, and there is no indication that it interferes in any way with the therapeutic action of sulphanilamide.—A. F. Hartmann, A. M. Perley and H. L. Barnett, *per Lancet*, i/1939, 403.

The practitioner is advised, if cyanosis appears, to adopt the following plan. (1) Administer methylene blue in pill form in a dose of 1 or 2 gr. thrice daily. (2) Continue the use of the sulphonamide preparation when clinically advisable, provided the patient is making progress apart from the cyanosis. (3) If cyanosis deepens, but no complaint is made, use Rubiazol in place of the sulphonamide previously employed: the dose should be 0.2 or 0.4 g. every four hours in adults. (4) When cyanosis progresses and sickness, lassitude, shallow breathing and mental distress appear, stop all sulphonamide preparations and have a spectroscopic examination of the blood carried out.—W. R. Snodgrass, *Practitioner*, i/1940, 22.

**DRUG FEVER.** In a series of 134 cases of various infectious conditions treated with sulphanilamide, a specific febrile reaction was encountered in 21 cases, which was accompanied by a rash in 9 cases. The average duration of the fever was from two to four days, with a definite prolongation in cases in which the drug was continued through the first few days of the reaction. In two cases, however, fever subsided in spite of the continued administration of the drug. Hepatitis with jaundice and stupor was present with the febrile response in one case.—P. O. Hageman and F. G. Blake, *J. Amer. med. Ass.*, ii/1937, 642.

**ENCEPHALOMYELITIS.** Two cases of encephalomyelitis, following the administration of sulphanilamide, one of which ended fatally. The total doses were small, 14 g. and 8 g. There is evidence that patients suffering from certain illnesses, including acute rheumatic fever and lupus erythematosus, are especially liable to develop toxic manifestations after taking sulphanilamide.—J. H. Fisher and J. R. Gilmour, *Lancet*, ii/1939, 301.

**GRANULOCYTOPENIA.** Granulocytopenia may occur after or during treatment with the sulphanilamide group of drugs. It has a high mortality rate. Routine leucocyte counts are not necessary in all patients receiving the drugs, but frequent blood examination should be made on all cases showing an atypical response to treatment. The duration of treatment is probably a more important factor than the total dosage of the drug. Details of ten cases of granulocytopenia following use.—F. D. Johnston, *Lancet*, ii/1938, 1044.

Serial leucocyte counts performed on 50 ambulant patients receiving 21 g. of sulphanilamide in 14 days, showed that in 46% of cases there was a transient polymorph leucopenia, and in 44% a monocytosis. These changes were usually found between the 7th and 20th day after administration of the drug.—C. J. C. Britton and J. Howkins, *Lancet*, ii/1938, 718.

Fatal granulocytopenia, following sulphanilamide therapy.—S. Berg *et al.*, *J. Amer. med. Ass.*, i/1938, 370. Another fatal case.—W. F. Schwartz, *ibid.*, 368; see also *ibid.*, i/1939, 823.

**HEPATITIS.** Five cases of toxic hepatitis due to sulphanilamide therapy.—C. F. Garvin, *J. Amer. med. Ass.*, ii/1938, 2283.

Death from acute yellow atrophy of the liver, following self-medication with sulphanilamide for gonorrhœal urethritis.—E. W. Clive, *J. Amer. med. Ass.*, ii/1938, 2384.

**METHÆMOGLOBINÆMIA.** Methæmoglobinæmia, resulting from sulphanilamide may be successfully combated by injections of methylene blue. In two children a

single injection of 1 mg. of methylene blue per kilo bodyweight reduced the methæmoglobin from 20% of the total pigment to less than 3% of the total in 45 minutes in one and from 18% to less than 3% in the other. The methylene blue has a catalytic action, accelerating the conversion of methæmoglobin to hæmoglobin.—W. B. Wendel, *J. Amer. med. Ass.*, ii/1937, 1216.

**OPTIC NEURITIS.** Toxic optic neuritis, in a girl of 16, resulting from treatment with sulphanilamide.—P. C. Bucy, *J. Amer. med. Ass.*, ii/1937, 1007.

**PORPHYRINURIA.** The available evidence would suggest that a certain degree of blood cell destruction is caused by sulphanilamide in the doses employed, but it is felt that the disturbance in pigment metabolism (porphyrinuria) is not to be explained by this fact alone. A more deep-seated effect upon the hæmopoietic system is suspected, analogous possibly in some ways to the toxic action of lead.—C. Rimington and A. W. Hemmings, *Lancet*, i/1938, 720.

Unpleasant symptoms and porphyrinuria decreased on administration of nicotinic acid in doses of 50 mg. three times a day. The most definite clinical change observed was a clearing of mental apathy so often present with the ingestion of sulphanilamide.—A. P. McGinty *et al.*, per *J. Amer. med. Ass.* i/1939, 1996.

**SKIN ERUPTIONS.** Two cases of toxic erythema, following use of sulphanilamide.—M. H. Goodman and C. S. Levy, *J. Amer. med. Ass.*, ii/1937, 1009.

Purpuric and scarlatiniform eruption, following the taking of a 5 gr. tablet.—I. L. Schonberg, *J. Amer. med. Ass.*, ii/1937, 1035.

A peculiar eruption induced by sulphanilamide and sunlight was produced experimentally in one patient, giving conclusive evidence that sulphanilamide was the photosensitising agent.—E. G. Ballenger *et al.*, *J. Amer. med. Ass.* ii/1937, 1057.

Cutaneous eruptions are more likely to occur in patients receiving large doses of sulphanilamide when they are exposed to constant rays of the sun. Details of four patients who developed skin eruptions.—J. G. Menville and J. J. Archinard, *J. Amer. med. Ass.*, ii/1937, 1008; L. J. Frank, *ibid.*, 1011; M. Salvin, *ibid.*, 1038.

Experience indicates that the presence of certain concentrations of sulphanilamide in the skin of susceptible individuals may contribute to a state of photosensitivity, and for this reason patients who are under treatment with this drug should be shielded from direct exposure to the rays of the sun.—L. A. Brunsting, *Proc. Mayo Clin.*, 1937, 614.

Sulphanilamide therapy may result in several distinct types of toxic dermatosis. The first and most common type is exposure to sunlight. In this type the level of sulphanilamide in the blood is not abnormally high, nor is there ordinarily a sensitivity to the drug. The second type is that in which definite sensitivity to the drug occurs, resulting in a sensitisation dermatitis. The patient cannot tolerate further sulphanilamide in any dose. The third type of dermatitis is that resulting from poor toleration of, or saturation with, sulphanilamide and presenting the typical picture of toxic dermatosis. The patient can tolerate further sulphanilamide therapy, providing excretory functions are normally resumed and the dosage is properly modified. There is no known sensitivity to the drug in these cases.—J. W. Tedder, *Arch. Derm. Syph.*, 1939, 224.

**SULPHÆMOGLOBINÆMIA** is a commoner consequence of sulphanilamide treatment than has hitherto been recognised, and is dangerous to anæmic subjects. Regular spectroscopic examination of the blood of all patients receiving sulphanilamide is therefore advocated. Details of eight cases of sulphæmoglobinæmia.—G. Discombe, *Lancet*, i/1937, 626.

Administration of magnesium sulphate simultaneously with, or during the two or three days preceding the administration of sulphanilamide, gives rise in most persons to sulphæmoglobinæmia. The formation of sulphæmoglobin takes place very rapidly, even after small doses of the drug. In the absence of sulphates large doses of the drug are tolerated, but in a considerable proportion of persons doses of 12 to 24 grammes per day result in methæmoglobinæmia. The removal of sulphæmoglobin from the blood is much slower than removal of methæmoglobin. The former has been detected 6 weeks after administration of sulphanilamide ceased. The latter disappears in about 24 hours. In sulphæmoglobinæmia oxygen is of little value, and blood transfusion is indicated.—J. P. J. Paton and J. C. Eaton, *Lancet*, i/1937, 1159.

While there is a good reason for avoiding sulphæmoglobinæmia, certain dietary restrictions seem to be based on a misconception. Thus it has never been shown that eggs in the diet promote the formation of sulphæmoglobin when the intestine

is normal, and the same applies to many other foods containing sulphur, many of which, such as cheese, contain more than eggs. When purgatives are given, however, the fluid contents of the small intestine are hurried into the colon, and it is the bacterial decomposition which takes place in these liquid faeces that produces the sulphides. Certain drugs, of which phenacetin is the most used, predispose to the formation of methæmoglobin and, if even small quantities of sulphides are present, of sulphæmoglobin. To sum up, therefore, when giving sulphanilamide and similar substances, purging and phenacetin should be avoided, but there is no reason why the patient should not have as normal a mixed diet as his condition allows.—*Lancet*, i/1940, 972.

**Pharmacology.** Sulphanilamide has a relatively low toxicity for animals and is almost entirely inactive pharmacologically. Large doses produce no alteration in blood pressure or on the action of the heart, and the smooth muscle of the uterus and intestine does not respond to the drug. On the whole it may be said to be well tolerated by tissues and organs.

Sulphanilamide given by the mouth is absorbed very rapidly, concentration in the blood being maximal in from three to four hours, followed by a gradual reduction in concentration, reaching zero in about 24 hours. It is absorbed entirely from the small intestine and not from the stomach. Neither subcutaneous nor intravenous injection increases the concentration in the blood and oral administration is the method of choice owing to its efficiency and simplicity, though the subcutaneous route has certain definite indications. The drug is very readily diffusible and rapidly finds its way, in almost equal concentrations, into all the secretions and tissues of the body (except bone and fat), including the salivary glands, the pancreas, the gall-bladder, the pleura, and the cerebrospinal spaces. In the cerebrospinal fluid the concentration is parallel with, and only slightly lower than in, the blood; indeed, the concentration of the drug in all parts attains a peak and diminishes *pari passu* with the concentration in the blood.

Excretion commences very shortly after administration; it begins within forty-five minutes, and the greater part is excreted within 24 hours. Excretion is almost entirely *via* the urine, partly as the free base and partly as the inactive acetyl compound. The excretion is dependent on the urinary flow and not on the blood concentration; it is, therefore, possible to wash out the drug by increased diuresis in the case of toxic symptoms occurring. It is important to note that the rate of excretion is slower in patients with renal damage.

To obtain the best therapeutic effect it is necessary to maintain a constant concentration of the drug in the blood, which is usually achieved by four-hourly administration. A blood concentration of 10 mg. per 100 ml. is necessary for the treatment of severe infections, and this may be obtained by a dosage of 1 g. per 20 lb. of bodyweight, or approximately 7 g. for a ten-stone man. Children and infants tolerate comparatively larger doses (*viz.*, from one-third to one-half the adult dose).

The mode of action of sulphanilamide still remains in dispute. It has been shown to have bactericidal action under certain conditions *in vitro*, this action being more marked in the presence

of blood or serum, and it has also been shown to exert a bacteriostatic effect *in vivo* in low dilutions and a bactericidal action in larger quantities. It is generally conceded, however, that this bactericidal action is too feeble to support the idea of a direct antiseptic action (though there is some evidence that the drug may be converted in the body into another product with much greater antibacterial activity). In view of the fact that it does not stimulate leucocytosis or phagocytosis, it is also improbable that it acts by directly fortifying the natural defence mechanisms of the body. It is suggested, however, on experimental evidence, that by rendering the blood and other tissue fluids unfavourable as media for the proper metabolism and active growth of susceptible bacteria it prevents the invasion of the tissues by these organisms, reduces the production of toxic substances, and thus assists the antibacterial mechanism of the body to effect recovery from the infection.

Pharmacological experiments show that sulphanilamide has almost no action on smooth muscle, heart or blood pressure. When very large doses are given to rabbits or cats it produces nervous symptoms somewhat resembling decerebrate rigidity.—Frank Hawking, *Lancet*, ii/1937, 1019.

In the dog, after administration of the drug, sulphanilamide is present in approximately equal concentrations in the various tissues with the exception of bone and fat. The distribution ratio, *i.e.*, the ratio of the concentration of the drug in the whole organism to the concentration in the blood, appears to be higher in man than in the dog. Simultaneous determinations of sulphanilamide in the blood and spinal fluid of man during several hours administration of the drug show that the concentration in the spinal fluid is parallel to and slightly lower than that of the blood.—E. K. Marshall, *J. Pharmacol.*, 1937, 61, 196.

The effectiveness of sulphanilamide therapy is related to the type of lesion. The function of the micro-organism, which is strikingly depressed by sulphanilamide, is its capacity to invade tissue. The effect of the drug on bacterial invasiveness seems to be influenced by the amount of debris present in the lesion. Sulphanilamide should be considered an agent which supplements, and in no way supplants, antibacterial immunity.—J. S. Lockwood, *J. Amer. med. Ass.*, ii/1938, 2259.

Free sulphanilamide is excreted in human breast milk in concentrations closely corresponding to the values present in the blood stream. A nursing baby cannot receive an adequate therapeutic dose through the milk of the mother receiving an average clinical dose.—H. L. Stewart and J. P. Pratt, *J. Amer. med. Ass.*, ii/1938, 1456.

It would seem that the amounts of sulphanilamide or acetylsulphanilamide excreted in human milk when therapeutic doses are given to the lactating mother, is not ordinarily harmful to the normal nursing infants.—S. S. Pinto, *J. Amer. med. Ass.*, ii/1938, 1914.

Sulphanilamide drugs do not stimulate leucocytic or phagocytic activity; they do not affect the speed of production or the quantity and quality of specific immune bodies; they are not instantly active and there is a quantitative relationship between the effective dose of the drug and the number of bacteria affected; they are active on highly virulent organisms, but inactive on "rough" organisms; they are not simple germicides, and they probably act by neutralisation of some metabolic function or enzymatic activity.—J. McIntosh and L. E. H. Whitby, *Lancet*, i/1939, 432.

In practice there are certain essentials which must be remembered in sulphonamide chemotherapy: (1) If the infecting microbe is insensitive to the drug no good can result. (2) Local administration has little hope of success. (3) If the infected dead material is present, elimination of the infection is not to be expected. (4) Bacteria in abscesses are little likely to be directly affected. (5) Administration of the sulphonamide drugs should render safe the excision of a wound infected with *streptococcus pyogenes*. (6) Valuable adjuvants to sulphonamide therapy in the treatment of septic wounds are (a) drainage of the infected walls of the



wound, (b) increase of immunity, especially by vaccines.—A. Fleming, *Proc. R. Soc. Med.*, 1940, 33, 136.

Pharmacology of the sulphanilamide group of drugs.—G. A. H. Buttle, *Brit. med. J.*, ii/1939, 269.

In the presence of the sulphonamide compounds, even in dilutions as great as 1 in 100,000, the pellicle formation on the surface of culture media, characteristic of the growth of *B. subtilis*, is inhibited, though there is no retarding influence on the rate of growth of the bacteria. The degree of inhibition of pellicle formation is known to be strictly parallel with the degree of inhibition of spore formation, and the inhibition and ultimate suppression of sporulation is indicative of sub-normal bacterial metabolism, showing that the bacteria are living in an asthenic state. This anti-bacterial activity of the sulphonamides may be designated "bacteriasthenicizing" activity.—M. Mandelbaum, *Nature, Lond.*, i/1941, 266.

**Uses.** Sulphanilamide was originally introduced into medicine for the treatment of streptococcal infections, especially those due to hæmolytic streptococci, and infections of this type still remain among its chief indications. Thus, it may be considered practically specific in the treatment of erysipelas, and its value has been established in puerperal sepsis, streptococcal septicæmia, tonsillitis, otitis media and mastoiditis, Ludwig's angina, cellulitis, lymphangitis, empyema, streptococcal arthritis and streptococcal peritonitis, and in scarlet fever in conjunction with antitoxin. It has proved dramatically successful in streptococcal meningitis, a condition which was hitherto almost invariably fatal. In streptococcal infections other than those due to *Str. hæmolyticus* it is of little value.

In addition to its value in streptococcal infections it has been used with marked success in a wide variety of conditions due to other infecting organisms. In meningococcal meningitis, for example, it has reduced the mortality rate from 30 to 50% to less than 10%. In the treatment of urinary tract infections, especially those due to *B. coli* or *B. proteus*, it gives results comparable with those obtained in streptococcal infections. It is remarkably effective against gonorrhœa and its complications, but the earlier enthusiasm for its use in these conditions has somewhat abated owing to the high relapse rate and the difficulty of ascertaining cure; nevertheless it still remains a valuable therapeutic weapon against gonococcal infections. In chancroid it may be regarded as a specific.

Gas gangrene due to *Cl. welchii* responds well to treatment with sulphanilamide, and recent work indicates its value, both orally and by local application, in the prophylactic treatment of infected wounds.

Sulphanilamide has also been employed in numerous other conditions with a varying measure of success, including actinomycosis, colds, endocarditis, gingivitis and other oral infections, malaria, measles, rheumatic fever, staphylococcal skin infections, trachoma, typhoid, and undulant fever.

It has been found of little value in pneumococcal infections, sulphapyridine (*q.v.*) being the drug of choice in these conditions.

### References to the More Important Uses of Sulphanilamide

In view of the vast amount of work which has been done during recent years on sulphanilamide it is impossible to give anything

approaching an exhaustive abstract review of this subject. It is hoped, however, that the numerous carefully selected abstracts contained in the following pages and taken from the more important papers which have appeared in this country and America, will prove sufficiently representative to convey an adequate appreciation of the use of this drug in the wide variety of diseases for which it has been advocated. Owing to the variations in dosage and technique of administration necessary to achieve the best results in different diseases, it has been thought desirable to preface the more important indications by a brief summary giving the essential details.

**ERYSIPELAS.** The efficacy of sulphanilamide as compared with other forms of therapy (e.g., ultra-violet light and scarlet fever antitoxin), may be gauged from the marked curtailment of the duration of spread of the rash, of the duration of the primary pyrexia, and of the duration of the toxæmia. There is usually a favourable response within 48 hours and a complete subsidence of symptoms within 10 to 14 days. It is best given in a dose of 1 g. at four-hourly intervals until the cessation of the primary pyrexia, and then in a dose of 0.75 to 1 g. three times daily until final cure is determined. To achieve the best results it is important to start administration before the third day of the disease. The drug may also be employed successfully in children, young babies being given 0.08 g. three or four times daily, older infants 0.15 g. two or three times daily, and older children 0.3 g. two or three times daily, the dose being reduced, but continued for a few days, after the fall of the temperature.

Prontosil is of undoubted value in the treatment of erysipelas. It is best administered by mouth in repeated doses in order to maintain the requisite concentration. It may be expected to produce a favourable result in about 48 hours, i.e., when about 60 gr. have been ingested. No obviously untoward results followed this dosage or mode of therapy. The drug ought to be persisted in for about a week.—G. E. Breen and I. Taylor, *Lancet*, i/1937, 1334.

A series of 312 cases was treated under controlled conditions with (a) ultra-violet light, (b) Prontosil, (c) ultra-violet light and Prontosil, or (d) scarlet fever antitoxin. The average case dosage of Prontosil was 5 g., and the average duration of Prontosil treatment two days (during the acute stage only). Those cases receiving Prontosil showed better results in respect of (i) curtailment of the duration of the spread of the local lesion, (ii) the duration of primary pyrexia, (iii) the duration of toxæmia.—W. R. Snodgrass and T. Anderson, *Brit. med. J.*, ii/1937, 101.

It also reduced the incidence of complications and diminished the tendency to recurrence. An effective method of treatment is to give 1 g. of sulphanilamide by mouth at four-hourly intervals until the cessation of primary pyrexia, and thereafter 0.75 g. thrice daily until final cure is determined.—W. R. Snodgrass and T. Anderson, *Brit. med. J.*, ii/1937, 1156.

A comparison of treatment by sulphamido-chrysoidine (Prontosil Rubrum), sulphanilamide (Streptocide), and benzylsulphanilamide (Proseptasine), in a controlled series of 242 cases. It was concluded that benzylsulphanilamide is not the drug of choice in the treatment of erysipelas, and that in this respect there is little to choose between sulphamido-chrysoidine and sulphanilamide. The dosage of the former should be 1.5 g. every 4 hours (9 g. daily) until the cure is established, then 1 g. three times daily for a further 14 days; and of the latter 1 g. every 4 hours (6 g. daily) until cure is established, and then 1 g. three times daily for a further 14 days.—W. R. Snodgrass *et al.*, *Brit. med. J.*, ii/1938, 399.

In a series of 162 patients treated with sulphanilamide the fatality rate was 2.46%; in 1193 cases treated during the years 1929 to 1933 the fatality rate was

13.4%. Sulphanilamide is the most effective form of therapy thus far used in the treatment of erysipelas.—A. L. Hoyne *et al.*, *J. Amer. med. Ass.*, ii/1939, 2279.

The effect of sulphanilamide on the course of facial erysipelas was studied in 42 cases, and compared with 43 similar cases treated previously by other methods. The drug was found to shorten the course of the illness and to decrease its extent and severity if it is administered before the third day of the disease, but it has little effect after this interval. Complications occurred frequently in the treated cases, but less often in those treated early. Recurrences and relapses occurred among the treated cases as often as among the untreated group.—L. A. Rantz and C. S. Keefer, *New Engl. J. Med.*, ii/1939, 809.

Adequate chemotherapy cures erysipelas in practically all cases within three or four days, the three preparations which have been most extensively used being Prontosil Rubrum, Rubiazol, and sulphanilamide.—T. Anderson, *Lancet*, ii/1939, 257.

**GAS GANGRENE.** Good results have been obtained from the use of 1 g. four-hourly for two or three days. (For prophylactic use see WOUNDS.)

Dramatically successful results in three cases. Conservative surgical principles should be combined with the use of sulphanilamide.—H. R. Bohlman, *J. Amer. med. Ass.*, ii/1937, 254.

Experimental evidence shows that bacteriostasis is the only demonstrable factor in the process which leads to the control of *Cl. welchii* infection in mice treated with sulphanilamide. Observations in experimental streptococcal infections in mice treated with sulphanilamide also indicate that bacteriostasis plays a role in the control of this type of infection.—E. A. Bliss and P. H. Long, *J. Amer. med. Ass.*, ii/1937, 1524.

In experimental infections in mice with *Cl. welchii* Type A, serum treatment was found better than sulphanilamide or sulphapyridine. In *Cl. septique* infection the best results were obtained when sulphapyridine was combined with serum, large doses of the drug being given immediately after infection and serum up to 24 hours later. In *Cl. oedematis* infection neither sulphanilamide nor sulphapyridine appears to have any influence.—D. Stephenson and H. E. Ross, *Brit. med. J.*, i/1940, 471.

The results obtained with sulphanilamide in cases of gas gangrene due to *Cl. welchii* have been so good that the extensive amputations commonly necessary in the last war for this condition may be largely avoided.—G. A. H. Buttle, *Lancet*, i/1940, 890.

**GONORRHOEA.** Considerable difference of opinion exists as to the best scheme of dosage, the best time to commence treatment, and the value of adjuvant treatment. It would appear advisable, however, to begin with fairly large doses, *e.g.*, 4 to 5 g. daily, in divided doses at four-hourly intervals for a few days, followed by 3 g. daily for a further week. Many workers are of the opinion that the institution of sulphanilamide treatment should be delayed until the 8th or 10th day of the disease, thus first enabling the tissues to develop a natural resistance to the infection, while others advocate the concurrent use of vaccine treatment with the same object in view. Auxiliary treatment by local irrigation may be advantageous in some cases. (More recently the use of sulphapyridine has tended to supplant the use of sulphanilamide in gonococcal infections.)

Treatment with sulphanilamide and Prontosil Soluble, combined with irrigations, proved efficient in 90 out of 100 cases, acute and chronic. In favourable cases of acute gonorrhoea cure is obtainable in about 15 days. Cases which do not react to Prontosil therapy within 18 days are not likely to react at all.—C. H. Andrews *et al.*, *Lancet*, ii/1937, 893.

Twenty-six out of 30 females and 91 out of 104 males affected with gonorrhoea were cured within 15 days by a course of treatment consisting solely of the oral administration of sulphanilamide and large quantities of fluids, the total dosage

of sulphanilamide given to each patient being 620 gr. during the period. No complications occurred.—H. Orr, *Canad. med. Ass. J.*, ii/1937, 364.

A series of 113 males and 101 females were treated for gonorrhœa. Of the males 68 were clinically cured in a fortnight, and a further 11 after a second course of sulphanilamide, a total of 70% in four weeks. Of the females 49 were free of symptoms in a fortnight, and a total of 66% within four weeks. The dosage used was 4.5 g. per day for the first few days, followed by 3 g. per day for six days. The complicated case responds as rapidly to sulphanilamide as the less advanced.—K. L. Evans, *Med. Pr.*, i/1938, 269.

It is better in all cases to wait until the attack has lasted for three weeks before starting treatment with any of these remedies.—L. W. Harrison, *Brit. med. J.*, ii/1938, 91.

Experience of 491 male cases and 142 female cases shows that the best results with sulphanilamide treatment in gonorrhœa can be obtained only by a specialised technique of administration (details of which are given). With this optimum technique (which includes vaccine treatment and the administration of sulphanilamide not before eight days from the commencement of symptoms), a permanent cure can be expected in 80% of male patients with one course of three weeks treatment (increased to over 90% with additional courses). Under optimum conditions the disease in women appears to react equally well to the drug.—A. J. Cokkinis and G. L. M. McElligott, *Lancet*, ii/1938, 355.

After the ordinary lavage treatment of gonorrhœa a normal spermatozoon count is the rule, but after sulphanilamide treatment only 39% of cases had a normal count. Cases with a very low spermatozoon count are found in 0.4% of patients treated by the ordinary method, but after sulphanilamide treatment 30% had a low count, verging on a state of azoospermia. This alteration in 50% of cases was still present after three months. In only one case was amelioration seen three months after cessation of treatment.—Jaubert and Motz, per *Lancet*, ii/1938, 1436.

An analysis of 1268 male and 210 female cases of gonorrhœa, whose chemotherapy was completed from 6 months to 2 years previously, showed that of cases with sulphonamide compounds (sulphanilamide, sulphapyridine or Uleron), and which have passed tests of cure about 20% relapse subsequently. The fact that half of these late relapses occurred more than three months after apparently complete cure, throws doubt on the reliability of certain published statistics of results obtained with sulphapyridine and other sulphonamide compounds.—A. J. Cokkinis and G. L. M. McElligott, *Brit. med. J.*, ii/1939, 1080.

Treatment of 1625 cases. Of unprecedented efficacy in the cure of gonorrhœa and its complications in the male.—B. Silver and M. Elliott, *J. Amer. med. Ass.*, i/1939, 723.

Confirmation of increased relapse rates in gonorrhœa, following treatment with sulphanilamide.—*Brit. med. J.*, ii/1939, 1204.

The use of sulphanilamide in gonorrhœa has thrown a deep cloud of uncertainty over the older tests of cure, and no matter how carefully these tests are carried out, some infected persons are almost sure to be passed back into sexual activity. Complement fixation tests are of little aid in the pronouncement of cure. Therefore, every patient should be warned against coitus without the use of a condom for some weeks after supposed cure.—P. S. Pelouze, *J. Amer. med. Ass.*, i/1940, 1878.

**MENINGOCOCCAL MENINGITIS.** The introduction of the sulphonamides has revolutionised the treatment of cerebrospinal fever and has radically improved the prognosis. Although sulphanilamide was the first in the field and has proved markedly successful, sulphapyridine (*q.v.*) is now considered the drug of first choice, since it is not only effective in the treatment of meningococcal and streptococcal infections, but is unique in its action in pneumococcal infection, and this is an advantage, since early administration is essential and the practitioner can rarely make a more precise diagnosis at the bedside than that the patient is suffering from a purulent meningitis. A scheme of treatment applicable either to sulphanilamide or sulphapyridine is therefore included under the latter drug.

Satisfactory clinical response in every one of 6 cases. A routine administration of sulphanilamide applicable in any of the severe coccic infections is as follows. (1) An initial subcutaneous injection of a large dose of the saturated (0.8%) solution is given in amounts approximating 0.05 g. per kg. (2) The drug is given by mouth every four hours day and night. (3) The dosage is graduated downward from an upper limit of 1 g. every four hours, depending on the size and age of the patient and the severity of the infection. (4) The drug is continued, in reduced dosage, for about ten days after symptoms and laboratory readings have returned to normal. (5) Sodium bicarbonate is given grain for grain with sulphanilamide to combat acidosis. (6) Magnesium or sodium sulphate is not given.—L. J. Willien, *J. Amer. med. Ass.*, i/1938, 630.

Sulphanilamide was used in the treatment of 10 cases. The response to treatment was good in all the patients and seemed quite comparable to that obtained with the specific antiserum.—F. F. Schwenker, *J. Amer. med. Ass.*, i/1937, 1407.

In view of the results so far obtained it seems reasonable to suggest that a patient with cerebrospinal fever should be given a dose of one of the sulphonamide products as soon as possible after diagnosis.—*Rep. med. Offr Minist. Hlth, Lond.*, 1938.

Twelve cases in children under 4 years treated with intrathecal and intramuscular injections of 0.8% sulphanilamide solution. The amount injected into the spinal canal was from 5 to 30 ml., according to the amount of spinal fluid withdrawn; the amount injected was less than the amount withdrawn. The intramuscular doses were from 35 to 150 ml., according to the weight of the patients. Of the 12 treated, 3 died (25%), the average fatality rate in the hospital for the previous six years, for children under 4, being 70%.—A. Eldahl, *Lancet*, i/1938, 712.

Ten children suffering from meningococcal meningitis were treated with sulphanilamide, and the cerebrospinal fluid became sterile in all cases. Four of the patients were less than a year old, and one of these died. All the 6 patients over a year old recovered.—T. Crawford and G. B. Fleming, *Lancet*, i/1938, 987.

Sulphanilamide therapy has changed the treatment of meningococcal meningitis from a difficult to a relatively simple matter. It is effective in Group II as well as in Group I infections. High initial dosage is advocated. The sulphanilamide level in the cerebrospinal fluid should preferably reach 5 mg. per 100 ml. in 24 hours and be maintained at this level for three days. Early cyanosis is not an indication for reducing dosage. The treatment is probably effective only in the acute stage. Clinical and experimental evidence so far is in favour of combined serum and drug therapy, especially in severe cases. Serum should be given in one or two large doses intravenously or intraperitoneally. Drainage is seldom required apart from daily lumbar punctures for two or three days. Report on 113 cases.—H. S. Banks, *Lancet*, ii/1938, 7.

Chemotherapy has revolutionised treatment and radically improved the prognosis. Cure may, as a rule, be obtained at all ages, is rapid, and with the single exception of deafness, is rarely accompanied by permanent sequelæ. The two drugs of proved potency, sulphanilamide and sulphapyridine, give equally good results when used in correct dosage. The dosage of sulphanilamide should be high, near the limit of tolerance, e.g., 9 g. a day for an adult, for 2½ to 3 days, and then very gradually reduced over the next 6 days. It should seldom be required and has little effect after the ninth day of treatment. Infants tolerate easily 3 g. a day for the first three days. The dosage of sulphapyridine should be similar but, since it is a more active drug, lower dosage is often effective. Serum is now unnecessary, even as an adjunct to chemotherapy.—H. S. Banks, *Lancet*, i/1940, 42.

In the Anglo-Egyptian Sudan the mortality of epidemic meningococcal meningitis often reaches 90%, but physicians working under the most adverse conditions have recently obtained by chemotherapy a survival rate of 90%.—F. G. Hobson, *Practitioner*, i/1940, 25.

**PUERPERAL SEPSIS.** Puerperal sepsis was among the first of the streptococcal infections treated by sulphanilamide, and the encouraging results obtained in early clinical trials were later substantiated by numerous workers. A dosage of from 3 to 5 g. daily is given until the temperature falls, and for a few days after, though in severe infections much larger doses have been advocated.

Its prophylactic value has not been so clearly established, and it is not recommended as a routine treatment in all cases, but only where there is a suspected or known risk of infection by hæmolytic streptococci, in which case a dose of 1 g. three times daily is suggested, beginning at the commencement of labour and continuing for three or four days.

#### *Curative.*

The aniline derivatives (originally Prontosil, and later Streptocide) have been used at the isolation block of Queen Charlotte's Hospital since January 1936, and it is now a routine practice to employ one or other of these drugs in every case of hæmolytic streptococcal infection. In the doses in which they have been given their use appears to be free from serious danger, and has been followed by a very great reduction in the mortality rate for these infections. There is good reason to believe that the treatment, rather than a change in the virulence of the organism, is responsible for the improvement, and there is every reason to continue the employment of these drugs until their value or otherwise is firmly established.—G. F. Gibberd, *Brit. med. J.*, ii/1937, 695.

A series of 106 cases treated with an average stay in hospital of 19.7 days, compared with 31.3 days in 1935. Although the death rate was 8%, only three deaths could be regarded as due to straightforward sepsis.—L. Colebrook and A. W. Purdie, *Lancet*, ii/1937, 1237, 1291.

22 cases treated with Prontosil Album in doses of 3 to 14.4 g. daily, continuously until the temperature fell, and thereafter for a few days. One patient died, giving a mortality rate for the whole series of 1.4% as compared with an average of 17.4% for a five-year period in the same hospital. In the recovered cases the fall in temperature and the general improvement were rapid.—M. A. Foulis and J. B. Barr, *Brit. med. J.*, i/1937, 445.

#### *Prophylactic.*

An investigation as to the prophylactic value of Prontosil Album, 140 patients being given the drug, and 162 being left untreated as controls. The drug was given in the third stage of labour, in most cases shortly before delivery, a daily dose of 2.7 g. being continued for a week. Analysis of the results showed little difference in the morbidity rate in the two series, but the only four cases of severe infection occurred in the controls.—B. Williams, *Lancet*, ii/1937, 343.

In view of the animal experiments and the bactericidal tests of women under treatment by sulphapyridine and sulphanilamide, the use of these drugs is suggested as a protective measure in maternity cases (and sometimes also in surgical cases) where there is believed to be special risk of infection by hæmolytic streptococci. The suggested dosage is 1 g. of sulphanilamide or of sulphapyridine thrice daily, beginning as soon as labour starts and continuing for 3 or 4 days.—E. W. Hoare, *Lancet*, i/1939, 76.

**UNDULANT FEVER.** The value of sulphanilamide in this disease has now been clearly established, the fever usually abating within a week or less, instead of after the usual period of months. A dosage of 3 g. daily has been recommended.

Two cases successfully treated.—L. A. Richardson, *Lancet*, i/1938, 495. See also A. E. Francis, *ibid.*, 496.

Three cases treated with prompt clinical cure. The maximum dosage (in tablet form), according to present standards, appears to be necessary.—R. L. Stern and K. W. Blake, *J. Amer. med. Ass.*, i/1938, 1550.

The use of sulphanilamide would appear to be a valuable aid in the diagnosis and treatment of human brucellosis. Animal experimentation indicates that in *Brucella* infections sulphanilamide markedly increases opsonocytaphagic activity for *Brucella* organisms.—H. Welch, *J. Amer. med. Ass.*, ii/1938, 226.

Two cases promptly and permanently cured.—E. F. Trant and C. E. Logan, *J. Amer. med. Ass.*, ii/1938, 1092.

Since undulant fever in man is a self-limited disease with a very limited case-mortality, it is doubtful whether the ordinary patient should be exposed to the dangers accompanying intensive treatment with sulphanilamide. No fewer than 7 out of 28 guinea pigs infected with *Br. abortus*, and receiving sulphapyridine by the mouth, died of toxæmia, and since both sulphapyridine and sulphanil-

amide have to be given for some weeks in a dosage bordering on the toxic limit if they are to bring about cure in guinea pigs infected with *Brucella*, attention is drawn to the grave danger attending the use of these drugs for more than a few days at a time, and it would seem wise to reserve this form of therapy for cases of undulant fever which have resisted other forms of treatment.—G. S. Wilson and I. Maier, *Brit. med. J.*, i/1940, 47.

**URINARY INFECTIONS.** Sulphanilamide can be expected to produce a cure in the vast majority of cases of cystitis and pyelitis due to *B. coli*, and it has the advantages over mandelic acid therapy of ease of administration, tolerance by the stomach, and the fact that it can be used during the acute stages of the disease. A further point in its favour is that it is effective in an alkaline urine, so that it is markedly bactericidal in infections due to *B. proteus ammoniae*. It may also safely be used in patients with impaired renal function, a condition which militates against the efficiency of other urinary antiseptics. The dose commonly recommended is 2 g. daily in divided doses, continued for five to seven days.

A comparison of mandelic acid and sulphanilamide as urinary antiseptics showed that sulphanilamide, because of its ease of administration and tolerance by the stomach, is the drug of choice in the average case, and it has the added advantage that it can be used during the acute stage of the disease. Acting best in an alkaline urine, sulphanilamide should be extremely useful in treating infections of the *Proteus* type, though its striking ineffectiveness in the treatment of *Streptococcus faecalis* infections is a definite handicap. These two drugs, one acting only in an acid, and the other best in an alkaline medium, supplement each other, and should be used in the treatment of urinary infections, according to the type or types of organisms causing them.—H. F. Helmholz, *J. Amer. med. Ass.*, ii/1937, 1039.

Sulphonamide given orally produces a urine strongly bactericidal for the organisms usually found in urinary infections, with the exception of *Streptococcus faecalis*. It is excreted in the urine, partly in the free state and partly as an acetyl derivative. If 30 gr. is given daily, on the third day the urine contains per 100 ml. about 100 mg. of free sulphonamide and 90 mg. of the acetyl compound. The latter is more actively bactericidal than the free substance in equal concentration, and its effect is much stronger in an alkaline urine, so that it is markedly bactericidal in infections due to *Proteus ammoniae*.—H. F. Helmholz and A. E. Osterberg, *Proc. Mayo Clin.*, 1937, 377; see also E. N. Cook and H. A. Buchtel, *ibid.*, 381.

It is a more potent antiseptic than mandelic acid and is effective in an alkaline urine; a bactericidal urine will develop in the presence of marked renal insufficiency. Coccal infections respond better than bacillary infections. In prostatitis, urinary infection associated with prostatitis, and in gonorrhoea, it has proved greatly superior to other antiseptics.—H. A. Buchtel and E. N. Cook, *Proc. Mayo Clin.*, 1937, 444.

Administration of sulphanilamide in doses of 0.5 or 0.6 g. by the mouth 3 times a day for 5 to 7 days effected rapid disappearance of *B. coli* and pus cells from the urine, and remission of symptoms in 46 women with urinary tract infections. Its simplicity of administration and rapidity of action make it especially invaluable in pyelitis of pregnancy and in the pre-operative treatment of gynaecological patients.—M. Kenny *et al.*, *Lancet*, ii/1937, 125.

Sulphanilamide has the advantage of rendering the urine slightly alkaline and can be used during the acute stages of pyelitis and cystitis. It is directly bactericidal and is more active in an alkaline medium. The sulphonamide groups of drugs is indicated in mixed infections and in the presence of haemolytic streptococci and *B. proteus*.—H. Droller, *Brit. med. J.*, ii/1938, 657.

A very efficient drug for the treatment of cystitis and pyelitis. The organisms which respond most readily are *B. coli*, *B. proteus*, and staphylococci.—D. R. Mitchell *et al.*, *Canad. med. Ass. J.*, i/1939, 336.

With suitable indications and in the right hands, sulphanilamide is capable of producing brilliant results in the treatment of non-specific urinary infections. Failures may be due to lack of proper identification of the infecting organism, since there are wide differences in the susceptibility of organisms within the

urinary tract to the action of sulphanilamide.—A. L. Clark, *J. Amer. med. Ass.*, i/1939, 719.

Sulphanilamide gives brilliant results in urinary infections in dosage considerably smaller than that required in the more aggressive septicæmic states. The ingestion of reasonable quantities of fluid does not seem to mitigate the beneficial action of the drug, provided adequate urinary concentration is obtained. The following is a representative dosage scheme: Infant, 1 g. daily; child of 6, 2 g. daily; adult 4 to 6 g. daily.—T. H. Crozier, *Practitioner*, i/1940, 516.

**WOUNDS.** Apart from its specific use in the treatment of gas gangrene, sulphanilamide has recently been widely advocated for the prophylaxis of wound infections, and the War Office has recommended its routine use in the presence of all wounds likely to become the site of secondary coccal or gas gangrene infection. The recommended dose is 1.5 g. in solution, followed by 0.5 g. two hours later, and then 0.5 g. four-hourly for four days. Sulphanilamide applied locally has also been found of value, usually in conjunction with oral administration, in checking bacterial growth in wounds. For this purpose it may be employed either as a dusting powder, as a pack, as a thick suspension, or as an irrigation (using a 0.8% solution). Local application to be effective must be given as soon as possible after infliction of the wound, since its value is markedly less when infection is well established.

#### *Oral Use.*

Where conditions favourable to general infection have arisen, prophylactic use of the sulphanilamide group should be valuable. Where infection has been established, the best therapeutic effects are secured in acute, diffuse conditions without marked local tissue changes. Hence, these drugs are not likely to obviate operative procedures where focal lesions such as accumulation of pus or extensive necrosis of bone or other tissues have occurred. Accordingly, powerful anti-septics, which act when brought into close contact with the organism locally, and which are relatively harmless to the tissues, will continue to be required also in the treatment of many septic infections.—C. H. Browning, *Brit. med. J.*, ii/1939, 265.

A provisional memorandum (A.M.D. 7, Oct. 11th, 1939) on the use of sulphonamide derivatives in the prophylaxis and treatment of wound infections, issued by the War Office to officers of the R.A.M.C., recommends that these compounds should be given a trial in the field, and that all wounds which appear likely to become the site of secondary coccal or gas-gangrene infection should receive a prophylactic course at the earliest opportunity, to be extended if infection supervenes.—*Lancet*, ii/1939, 996; *Brit. med. J.*, ii/1939, 969.

The recommendations of the War Office for the prophylactic use of sulphanilamide in war wounds are in the main supported. It is recommended that the first dose should be 1.5 g. given in solution for rapid absorption, and that the succeeding 0.5 g. doses, starting 2 hours after the first dose, should be given four-hourly as intact tablets to prolong their effect. It is essential that the first dose be given as soon as possible after wounding, to combat the gas-gangrene organisms, and prophylaxis must be continued for at least four days. If several hours have elapsed before treatment begins the first few doses should be increased.—A. T. Fuller and G. V. James, *Lancet*, i/1940, 487.

Because of its availability, cheapness, and low toxicity, sulphanilamide should be used in most cases, sulphapyridine being reserved for chest wounds, and sulphathiazole for staphylococcal infections. A prophylactic course should be given in all patients with wounds severe enough to carry a risk of dangerous infection. A first dose of three crushed tablets of sulphanilamide (1.5 g.) is given with a cup of hot lemonade, a single tablet is given two hours later, and thereafter one tablet four-hourly up to the end of the fourth day, making 13.5 g. in all. After the first 24 hours a double dose may be given the last thing at night to allow eight hours uninterrupted sleep. The course should be continued after debridement, or begun if it is not already in operation. If infection has already appeared the above doses should be doubled. The chief danger of prolonged administration is leucopenia; a differential blood count on a blood smear should be made



at the end of the first week, and then every three days; a drop in polymorphs to less than 50% is an indication that the drug should be stopped.—W. H. Ogilvie *Practitioner*, ii/1940, 337.

#### Local Use.

Experiences of the fighting in France and Belgium (1940) have proved the value of sulphonamide as a local application for checking bacterial growth in wounds. The wound should be thoroughly dusted with sulphonamide powder (preferably with a hand-operated air-pump) as early as possible, and a single dose of 2 g. given by the mouth at the same time. There should be a second dusting after debridement if this is carried out many hours after the first treatment. When there is reason to fear late infections, this treatment should be followed up by administration of the drug by the mouth on the lines recommended in the War Office Memorandum of July 3rd, 1940.—L. Colebrook, *Lancet*, ii/1940, 113.

The best method of administering sulphanilamide for local use is by means of a thick suspension, prepared by adding 2 g. of powdered sulphanilamide to 100 ml. of a 0.8% solution of sulphanilamide in physiologic saline solution. This is the compound of choice when dealing with infections caused by *B. coli*, hæmolytic streptococci, *Cl. Welchii*, or *Neisseria intracellularis*, but for infections due to pneumococci or staphylococci, sulphathiazole or sulphapyridine are preferable. Local application should be carried out at least three times daily. When treating fractures or fracture wounds, the powdered substance is placed directly in the wound as a heavy dressing powder prior to the application of a cast. The treatment is of greater value for the prevention of an infection than in an already well established infection.—W. E. Herrell and A. E. Brown, *Proc. Mayo Clin.*, 1940, 611.

The irrigation of infected or potentially infectible wounds (especially following posterior resection or combined abdominoperineal resection for carcinoma of the rectum) by a solution of sulphanilamide has given satisfactory results. The solution employed is prepared by heating a physiologic solution of sodium chloride to the boiling point and adding sufficient sulphanilamide to make a saturated solution (0.8% is the limit of solubility). Irrigations are started after the posterior pack, inserted at the time of operation, has been removed. Flushing the cavity with hydrogen peroxide before irrigation with the solution of sulphanilamide was found to be a useful adjunct. The irrigations are done three times a day.—C. W. Mayo and J. M. Miller, *Proc. Mayo Clin.*, 1940, 609.

Local application has been advocated under two conditions, as a field dressing and as a pack after debridement. In the first case, powder, tablets, or cylinders of sulphanilamide are inserted well into the wound when the first field dressing is applied, and in the second the powdered drug is dusted thickly over the surface of the excised wound, which is then lightly sutured or packed with sterile gauze over the powder. In either case the largest amount that should be used is 15 g. (roughly three dessertspoonfuls of the powder). Sulphanilamide used locally at a time when the bacteria are still limited to the wound track attains its maximum concentration where it is most wanted. It is also absorbed and appears in the circulation in bacteriostatic quantities for about 48 hours. After this time oral administration should be started. Once infection is established in a wound the drug is less effective as a local application than when given by mouth.—W. H. Ogilvie, *Practitioner*, ii/1940, 337.

#### Miscellaneous References

ACTINOMYCOSIS. A remarkable recovery following the use of 1 g. thrice daily by mouth.—O. Walker, *Lancet*, i/1938, 1219.

A case successfully treated.—E. M. Miller and E. H. Fell, *J. Amer. med. Ass.*, i/1939, 731.

Three cases completely cured.—L. Dobson *et al.*, *J. Amer. med. Ass.*, i/1941, 272.

BACTERIAL ENDOCARDITIS. Sulphanilamide therapy had no effect on the general course of 13 cases of subacute bacterial endocarditis. The main beneficial effect was a fall in the number of bacteria in the blood stream. It did not prolong the life of the patients in this series, and there is some evidence that it may have actually shortened the time of survival.—H. H. Steele, *New Engl. J. Med.*, ii/1940, 1067.

Best results when combined with heparin therapy and hyperthermia. Review of 200 cases.—S. S. Lichtman and W. Bierman, *J. Amer. med. Ass.*, i/1941, 286.

**BURNS.** For serious burns the Ministry of Health recommends (after cleansing of the burn) a light dusting of sulphanilamide powder prior to application of coagulant or (in the treatment of burns on the face and hands) of Tulle Gras.—*Pharm. J.*, i/1941, 77.

**CHANCROID.** 20 cases successfully treated. Each case received 5 ml. of Prontosil Soluble 5% injected deep-subcutaneously over the gluteus medius, and one or two further injections at 3-day intervals of 10 ml., with Prontosil Album by mouth in divided doses, 3 g. in 24 hours. There was rapid healing of ulcer without leaving the old precipitous-edge scar. After circumcision and extirpation of frenum there was never a sign of chancroid infection of the cut surfaces.—H. M. Hanschell, *Lancet*, i/1938, 886.

A rapid cure effected in every one of 10 cases, four of which had relapsed after Dmelcos vaccine intravenously. The good results of treatment appear to be permanent.—R. C. L. Batchelor and D. Lees, *Brit. med. J.*, i/1938, 1100.

A series of 45 cases successfully treated, treatment consisting of the administration of 80 gr. of the drug in divided doses for the first five days, and 40 gr. in divided doses for nine additional days. Without exception, the treated cases healed promptly at the end of two weeks.—B. A. Kornblith, *J. Amer. med. Ass.*, ii/1938, 523.

Treatment with sulphanilamide or sulphapyridine cures rapidly, a daily dose of 2 to 3 g. of the latter for 5 to 10 days is sufficient to produce a cure. Intravenous injections of Dmelcos vaccine may also be used, but this causes severe systemic upset.—Robert Lees, *Med. Pr.*, 1939, 615.

This drug is efficient even in resistant cases, and if carefully controlled can be used with gratifying results. The average time required for healing in a control group was 32 days, compared with an average of 15.7 days for the sulphanilamide-treated group.—W. F. Schwartz and H. E. Freeman, *J. Amer. med. Ass.*, i/1940, 986.

**COLDS.** Sulphonamide by the mouth is effective in cutting short primary infective colds of more than two days' duration, and virus colds in the stage of secondary infection. It has no action in the virus stage.—A. L. Yates, *Canad. med. Ass. J.*, ii/1939, 275.

**GINGIVITIS.** The obvious manifestations of acute gingivitis, whether localised or diffused, could be made to clear up completely in about a week by oral administration of sulphanilamide or sulphapyridine, 3 to 4 g. daily. The fœtor and the morning stain on the lips and teeth completely disappeared. The œdematous interdental papillæ shrank, and the large lymph glands observed in some cases subsided. But it was quite certain that one course of chemotherapy did not cure gingivitis, the condition relapsing a week or so afterwards. By giving further courses, however, and particularly by increasing the immunity response by vaccine therapy, the infection could be indefinitely delayed for 6 months or more.—A. J. Cokkinis, *Brit. med. J.*, ii/1939, 1158.

**GONORRHOEAL ARTHRITIS.** The end-results in 18 cases treated by sulphanilamide were more satisfactory, and took place in shorter periods of time, than occurs with other forms of therapy.—H. C. Coggeshall and W. Bauer, *New Engl. J. Med.*, i/1939, 85.

**HÆMOLYTIC STREPTOCOCCAL MENINGITIS.** The use of sulphanilamide in these cases has yielded the most revolutionary results. Prior to its use the case fatality was more than 95%; since its use the rate has been less than 20% in a group of 27 cases.—J. B. Neal, *J. Amer. med. Ass.*, ii/1938, 1353.

Recovery of a case of streptococcal meningitis after injection of Prontosil.—M. J. L. Frazer, *Brit. med. J.*, i/1937, 1022.

**MALARIA.** As a result of treatment of 80 unselected cases of acute malaria it was concluded that sulphanilamide is much less efficient than quinine, is more dangerous, and is much more costly.—J. C. Niven, *Trans. R. Soc. trop. Med.*, 1938, 32, 413.

Prontosil is not a practical addition to the therapeutic armament against malaria; it is much less efficient than quinine, is more dangerous and is much more costly.—J. C. Niven, per *Trop. dis. Bull.*, 1940, 134.

**MEASLES.** Sulphanilamide is of some value in shortening the duration of bronchopneumonia, but has little effect on the course of the other main complications of measles, with the possible exception of otitis media.—T. Anderson, *Brit. med. J.*, i/1939, 716.

**ORAL INFECTIONS.** Sulphanilamide has been packed into tooth sockets (2½ gr.

per socket) after extractions for pyorrhœa or periapical infection in more than 350 cases, with prompt bactericidal effect and no complications.—W. D. Lanier, *J. Amer. pharm. Ass., pharm. Abstr.*, 1939, 158.

**OTITIS MEDIA.** During the past year (1938) all cases of acute suppurative otitis media at the Royal Naval Hospital, Chatham, have been given, immediately on admission, "Colsulanyde," 1 drachm four-hourly by mouth, in addition to the usual treatment for acute ear, and during this period the ratio of acute mastoiditis to acute otitis media has been reduced from 22·7 to 4·5%. The sulphonamide group of drugs has a very real place in the treatment of acute suppurative otitis media.—V. G. Horan and S. G. French, *Brit. med. J.*, ii/1938, 942.

Sulphanilamide therapy should be continued until there is bacteriological as well as clinical evidence of complete subsidence of infection, and the laboratory studies required for its effective use necessitate hospitalisation of patients under treatment. The therapy should be reserved for the treatment of spreading or life-endangering streptococcal infections.—J. M. Converse, *J. Amer. med. Ass.*, ii/1939, 1383.

A series of 621 cases of acute suppurative otitis media treated with sulphanilamide over a period of two years. The incidence of mastoiditis was only 3·4% compared with 22·7% before the introduction of treatment with sulphanilamide. It is urged that all cases of suppurative otitis media should receive sulphanilamide or sulphapyridine. This will greatly reduce the incidence of mastoiditis and will allow a more conservative attitude to be adopted once mastoiditis develops.—V. G. Horan and S. G. French, *Lancet*, i/1940, 680.

**RHEUMATIC FEVER.** The prophylactic use of sulphanilamide may avert the risk of rheumatic fever, following tonsillitis. Thomas and France gave sulphanilamide continuously through two winters (15 to 20 gr. daily for seven months without ill effects) to 30 patients with a recent history of acute rheumatic fever. None had major attacks of acute rheumatic fever, or an acute  $\beta$ -hæmolytic streptococcal infection, while taking sulphanilamide. Of 30 control patients, 4 developed 5 major attacks during the same period, 1 was admitted to hospital with an acute streptococcal infection, and 3 had acute illnesses which might have been of a rheumatic character.—J. A. Glover, *Lancet*, i/1939, 465; see also C. B. Thomas *et al.*, *J. Amer. med. Ass.*, i/1941, 551.

**SCARLET FEVER.** In a series of strictly controlled cases of scarlet fever during the period July 1936 to May 1937, the administration of sulphonamide was found to have no significant effect upon the duration of the initial pyrexia, the incidence of toxæmia, or the incidence of complications.—J. C. Hogarth, *Brit. med. J.*, ii/1937, 1160.

Collected experience suggests that whereas the initial toxæmia of scarlet fever, as evidenced by pyrexia, malaise, vomiting and rash, are unaffected by the sulphonamide drugs, a combination of chemotherapy with antitoxin will give the best results. Although the most effective drugs appear to be sulphanilamide and sulphapyridine, Proseptasine and Soluseptasine are less toxic, and may with greater safety be given in larger doses over longer periods.—A. R. Thompson, *Practitioner*, i/1940, 54.

**STAPHYLOCOCCAL INFECTIONS.** In multiple skin lesions the drug has no effect but when the infection is a localised one, as in carbuncles, solitary boils, furuncles of the nose or external auditory meatus, styes or whitlows, the results are often astonishingly good. Boils, furuncles and whitlows generally heal in about three days, and carbuncles in about 7 to 10 days. Treatment must be started early, before necrosis has occurred, dosage being from 1·5 to 2 g. daily *per os*.—M. Marcus, *Brit. med. J.*, ii/1938, 92.

**TONSILLITIS.** It would not seem wise to give sulphonamide indiscriminately to child patients with uncomplicated tonsillitis. At the slightest sign of spread, however, to the ears, cervical glands, or lower respiratory tract, the drug should be given in full doses. If a throat swab shows that the organism present is the hæmolytic streptococcus, then one of the sulphanilamide preparations should be used. In the absence of bacteriological certainty, however, sulphapyridine should be chosen.—A. Moncrieff, *Practitioner*, ii/1939, 429.

In a series of 31 sulphanilamide-treated patients and 36 controls, this drug was found not to reduce the severity of the symptoms, shorten the period of incapacity, reduce the incidence of complications, or reduce the duration of the carrier state. In the average uncomplicated case of tonsillitis or pharyngitis, due to hæmolytic streptococci, the advisability of its routine use is questionable.—P. S. Rhoads and M. L. Afremow, *J. Amer. med. Ass.*, i/1940, 942.

**TRACHOMA.** Rapid improvement, both of subjective and objective symptoms, in 140 cases.—F. Loe, *J. Amer. med. Ass.*, ii/1938, 1371.

**TYPHOID BACILLURIA.** A case of typhoid pyelitis and bacilluria, which failed to respond to hexamine and ammonium mandelate, was treated with sulphanilamide. After five days' treatment culture was negative, but typhoid bacilluria returned when sulphanilamide treatment was discontinued. The urine became sterile after four further days' treatment, and after a course of sulphanilamide lasting fourteen days, there was no recurrence of bacilluria.—M. Barer, *Lancet*, ii/1937, 964.

**ULCERS.** Treatment of ulcers infected with streptococci with the following paste is recommended. Benzoic acid 0.2%, sulphanilamide 0.8%, glycerin 10%, powdered tragacanth 10%, in Ringer's solution.—B. Fantus and H. A. Dyniewicz, *J. Amer. pharm. Ass.*, 1939, 548.

**VULVOVAGINITIS.** In a series of 25 patients suffering from gonorrhœal vulvovaginitis, who were given sulphanilamide (after other treatments had failed), 7 were cured in an average of 17.3 days, and 9 in an average of 42.9 days; only two of the remaining 9 were cured by additional administration of sulphanilamide.—S. J. Hoffman *et al.*, *J. Amer. med. Ass.*, i/1938, 1541.

[P1.81.84] **Prontosil Rubrum** (Bayer Products, London). *Syn.* PRONTOSIL FLAVUM, SULPHAMIDOCHRYSOIDIN.

$(\text{NH}_2)_2 \cdot \text{C}_6\text{H}_3 \cdot \text{N} : \text{N} \cdot \text{C}_6\text{H}_4 \cdot \text{SO}_2 \cdot \text{NH}_2 = 291.3$ .

*Dose.*— $7\frac{1}{2}$  to  $22\frac{1}{2}$  grains (0.5 to 1.5 g.). The child's dose is one half and the infant's dose one-third of these quantities. Both Prontosil Rubrum and Prontosil Album can be given in treatment combined with injections of Prontosil Soluble. With clinical improvement the injections are abandoned, treatment continuing with tablets alone, the daily intake of which is gradually reduced. In moderately severe cases the dosage for combined treatment is as follows:—Prontosil Soluble solution (5%) 10 to 15 ml. per 24 hours with Prontosil Rubrum or Prontosil Album 0.5 to 1 g. thrice daily. In severe cases, the amount of Prontosil Soluble solution (5%) should be increased to 20 to 25 ml. per 24 hours.

Prontosil Rubrum consists of 4-sulphonamido-2 : 4-diaminoazobenzene. It is a red crystalline powder and is supplied both in powder and in tablets containing  $7\frac{1}{2}$  grains (0.5 g.) for oral administration. This is the original product and was first marketed under the name Prontosil. Although to a great extent it has been superseded by sulphanilamide and other derivatives, some practitioners consider that its action is more reliable than that of sulphanilamide itself.

Almost *insoluble* in water; soluble about 1 in 7 of acetone; moderately soluble in alcohol and soluble about 1 in 11 of a mixture of equal parts of alcohol (95%) and acetone. Prontosil Rubrum also dissolves in dilute hydrochloric acid, forming a hydrochloride melting at  $248^\circ$  to  $250^\circ$ , and slightly soluble in cold, but easily soluble in hot water. The hydrochloride has also been used therapeutically.

Stains caused by Prontosil Rubrum on undyed linen articles can be removed by rinsing the article in a dilute aqueous solution of sodium thiosulphate. Woollen articles should be treated with acetone and then washed repeatedly in luke-warm water.

*Uses.* Prontosil Rubrum is used for similar purposes to sulphanilamide and with comparable results. In the body it is partly broken down to sulphanilamide and partly excreted unchanged,

but there is some evidence that its activity is not dependent on its sulphanilamide content. It is excreted more slowly than sulphanilamide and is stated to be less toxic.

Prontosil Rubrum is used as a local application in cases of boils, carbuncles, infected wounds and cavities, breast abscesses, cellulitis, tonsillitis, erysipelas, etc., in the form of lotion, ointment or powder. Lotions of from 1 to 10% strength may be prepared by dissolving the drug in a mixture of equal parts of alcohol and acetone containing 1% of glycerin. A suitable ointment consists of Prontosil Rubrum 5 parts, liquid paraffin 25 parts, and wool fat 10 parts. When used in the form of a powder, 1 part of Prontosil Rubrum may be diluted with 10 parts of lactose.

[P1-S1-S4] **Prontosil Soluble** (*Bayer Products, London*). *Syn.* PRONTOSIL-S, NEO-PRONTOSIL.

$C_{18}H_{14}O_{10}N_4S_2Na_2 = 588.5$ .

*Dose.*—10 to 25 ml. of a 5% solution per 24 hours by intramuscular injection.

Prontosil Soluble is the disodium salt of 4'-sulphonamido-phenylazo-7-acetyl-amino-1-oxynaphthalene-3, 6-disulphonic acid, supplied in 5 and 10 ml. ampoules of 5% solution for intramuscular injection.

**Soluble** 1 in 25 of water, but insoluble in alcohol, acetone, chloroform and ether.

**Uses.** The solution of Prontosil Soluble is recommended for use in conjunction with oral administration of Prontosil Album or Prontosil Rubrum, except in urinary tract infections, erysipelas, mild conditions and prophylaxis, where oral therapy alone suffices. Suggested dosages for the combined treatment are given under Prontosil Rubrum. It is important that Prontosil Soluble be given only by the intramuscular route, since intravenous injection is not without risk and appears to be no quicker in effect.

Prontosil Soluble may be used with 20% glycerin as a paint for the mucous membrane, and it has been used alone as a paint and gargle. An isotonic solution for use in the eye, etc., may be prepared by diluting the 5% solution of Prontosil Soluble with an equal amount of sterile saline.

[P1-S1-S4] **Proseptasine** (M & B 125) (*Pharmaceutical Specialities (May & Baker) Ltd., London*). *Syn.* BENZYL-SULPHANILAMIDE.  $C_6H_5 \cdot CH_2 \cdot NH \cdot C_6H_4 \cdot SO_2NH_2 = 262.32$ .

*Dose.*—Prophylactic, 0.5 g. every four hours. In treatment of septicæmic conditions, 1 to 2 g. every four hours until the temperature has been reduced. Thereafter 0.5 g. every four hours for 4 days or longer. In scarlet fever and streptococcal tonsillitis the initial dosage is 1 g. every four hours for 48 hours, and thereafter 0.5 g. every four hours for 4 days or longer. Proseptasine can be combined with injections of Soluseptasine, when the modified dosage forms indicated under Soluseptasine should be followed. Children receive half to three-quarters and infants up to 2 years a quarter to a half of the adult dose.

Proseptasine is *p*-benzylaminobenzenesulphonamide, a white, odourless, tasteless powder. It is supplied in the form of tablets, each containing 0.5 g. for oral administration.

Slightly *soluble* in water (1 in 1000), but more soluble in alcohol, acetone and dioxane. Proseptasine crystallises from solutions in acetone and dioxane when they are diluted with water.

**Uses.** The indications for its use are similar to those for sulphanilamide, but it is stated to be much less toxic. Its solubility is low, hence no large amounts can be absorbed from the intestinal tract at any one time, and its activity in equal doses is lower than that of sulphanilamide.

**MEASLES.** There is evidence that Proseptasine is of value in reducing the incidence of complications due wholly or in part to secondary invasion by hæmolytic streptococci, the best results being obtained in pure streptococcal complications, such as otitis media.—J. C. Hogarth, *Brit. med. J.*, i/1939, 718.

**STREPTOCOCCAL INFECTIONS.** The administration of Proseptasine to scarlet fever patients reduced the number of patients having complications from 56% in the control series to 35%. In erysipelas the spread of the disease was arrested in 24 hours in all of 47 cases.—B. A. Peters and R. V. Havard, *Lancet*, i/1937, 1273.

[P1·81·84] **Soluseptasine** (M & B 137) (*Pharmaceutical Specialities* (May & Baker) Ltd., London).  $C_{15}H_{16}O_6N_2S_3Na_2 = 494.5$ .

**Dose.**—By intramuscular or subcutaneous injection, 5 ml. of a 5% solution every 4 to 6 hours, the maximum dose in 24 hours not exceeding 30 ml. For children, 3 ml. should be administered at each injection. By intravenous injection, an initial dose of 5 ml. of a 5% solution should be given to test the tolerance of the patient, followed some 4 hours later by a further injection of 10 to 20 ml. Injections should be administered slowly. The dose of 10 to 20 ml. may be given twice or even oftener in the course of 24 hours, if necessary. Injections of Soluseptasine may be combined with oral administration of Proseptasine. One or more daily injections of 5 ml. of 5% solution of Soluseptasine are supplemented by the ingestion of 0.5 to 1 g. of Proseptasine at four hourly intervals. In this combined treatment more than 4 g. of Proseptasine should not as a rule be given in the course of 24 hours. For children, 5 to 10 ml. of 5% Soluseptasine solution may be injected intravenously with a total of 20 ml. in 24 hours, supplemented by 0.5 g. of Proseptasine by mouth every four hours.

Soluseptasine is disodium-*p*-( $\gamma$ -phenylpropylamino)-benzenesulphonamide- $\alpha,\gamma$ -disulphonate. It is a white crystalline powder, *soluble* in water to give an almost neutral solution.

**Uses.** Soluseptasine is used for similar purposes to Proseptasine and may be employed either alone or in conjunction with the latter. It is also supplied in the form of an ointment for use in varicose ulcers, skin infections, infected wounds, and as an adjuvant to oral or injection treatment in erysipelas and cellulitis; and in the form of a spray containing 10% of the active substance in glycerin for use as an application in infections of the ear, nose and throat.

[P.1.81.84] **Uleron** (*Bayer Products, London*). *Syn.* DISEPTAL A.  $\text{NH}_2\cdot\text{C}_6\text{H}_4\cdot\text{SO}_2\text{NH}\cdot\text{C}_6\text{H}_4\cdot\text{SO}_2\text{N}(\text{CH}_3)_2 = 355\cdot42$ .

*Dose.*— $7\frac{1}{2}$  to 15 grains (0.5 to 1 g.) thrice daily after meals. Children receive half and infants up to 2 years a quarter of the adult dose. If delayed onset of action points to some difficulty in absorption, it is advisable to administer the preparation with alkaline media, such as sodium bicarbonate or soda water, since Uleron is soluble in an excess of alkali.

Uleron consists of 4-(4'-aminobenzenesulphonamido)-benzenesulphondimethylamide, a colourless substance with a slightly bitter taste, issued in  $7\frac{1}{2}$  grain (0.5 g.) tablets. Also available as an ointment (5%).

**Soluble** with difficulty in water; readily soluble in alkaline solvents such as dilute caustic soda; also soluble in alcohol and acetone.

**Uses.** This drug was first introduced in 1937 as the result of an endeavour to find a substance which would influence the largest number of diseases, apart from streptococcal infections. It was found particularly effective against gonococcal infections, and has been widely used in Germany in the treatment of gonorrhoea, both in males and females. In spite, however, of the early enthusiastic reports, it appears to suffer from certain disadvantages, namely, (1) that it is generally considered that treatment with the drug must be delayed until the second week of the disease, (2) that adjuvant therapy, in the shape of vaccines and irrigations, is advised, and (3) that unless the dosage and time schedule is strictly adhered to there is a danger of peripheral neuritis occurring. It has been found, moreover, that chronic cases respond better to the drug than acute cases.

The essential feature of Uleron therapy in gonorrhoea is that it must be carried out in the form of short courses, *i.e.*, it is administered for 3 to 4 days (at the most 5 days), after which an interval of at least 6 (preferably 8) days is allowed to elapse. A second course may then be given and, if necessary, after another interval, a third course. The total dose for each of these short courses must not exceed 12 g. (or exceptionally 15 g.). If gonococci are still found after these three courses other measures of treatment must be adopted.

Provided the dosage scheme outlined above is adhered to, the drug is usually well tolerated, and the minor toxic effects common to sulphonamide therapy are rarely encountered; if these should occur, however, the use of the drug must be suspended immediately and its further use withheld.

Polyneuritis in a man of 63, following administration of 16 g.—C. T. Valkenburg and G. A. K. von dem Borne, *Lancet*, ii/1938, 889.

**GONORRHOEA.** Uleron is definitely a most valuable adjuvant in the treatment of gonorrhoea, and when the optimum dosage is established a high percentage of cures should be possible within three weeks. Non-acute cases seem to respond more readily than acute cases.—D. F. Walsh, *Brit. med. J.*, ii/1938, 215.

Uleron does not exhibit marked efficacy in recent gonorrhoea, and it is usually recommended that treatment be delayed until the second week of the disease,

when sufficient time has elapsed for the tissue defences to be marshalled. Prior to the start of and during chemotherapy, gonococcal vaccines and local treatment are both advised. With this compound it is essential to limit treatment to short periods of four days only; the excretion of Uleron is slower than other sulphonamides. A second course of treatment is required in most cases after an interval of a week, and in some a third course may be necessary. Uleron has the marked disadvantage of causing peripheral neuritis if the short period schedule is not rigidly followed.—V. E. Lloyd, *Practitioner*, i/1940, 48.

[P1-81-84] **Albucid** (*Schering, London*).  $\text{NH}_2\cdot\text{C}_6\text{H}_4\cdot\text{SO}_2\cdot\text{NH}\cdot\text{COCH}_3 = 214\cdot2$ .

*Dose*.—A single course of 1·5 g. (22½ grains) thrice daily for seven consecutive days is stated to be effective in the treatment of gonorrhœa. If necessary the course may be repeated after an interval of eight days. For women the dose is 1 g. (15 grains) thrice daily, and for children 0·5 g. (7½ grains) thrice daily.

Albucid is *p*-aminobenzenesulphonacetamide.

The compound is also effective in the treatment of coli or staphylococcal infections of the urinary tract, the dose being 2 tablets thrice daily.

[P1-81-84] **Ambesid-Solubile** (*Richter, London*).

$\text{COONa}\cdot(\text{CH}_3)_2\text{CO}\cdot\text{NH}\cdot\text{C}_6\text{H}_4\cdot\text{SO}_2\text{NH}_2 = 294\cdot3$ .

*Dose*.—0·8 to 1·2 g. (12 to 18 grains) thrice daily. Max. adult daily dose 5 g. (75 grains). By injection an average daily dose of 2 to 10 ml. of a 10% *w/v* solution can be administered intramuscularly or intravenously.

Ambesid-Solubile is the sodium salt of succinyl-*p*-aminobenzenesulphonamide.

Advocated for the same purposes as sulphanilamide, but is stated to be more readily absorbed owing to its greater solubility.

[P1-81-84] **Syrup Ambesid** (*Richter, London*) contains 4 grains of Ambesid-Solubile in 2 fluid drachms.

[P1-81-84] **Rubiazol** (*Roussel Laboratories, London*).

$(\text{NH}_4)_2\cdot\text{C}_6\text{H}_4\cdot\text{COOH}\cdot\text{N}\cdot\text{N}\cdot\text{C}_6\text{H}_4\cdot\text{SO}_2\text{NH}_2 = 335\cdot3$ .

*Dose*.—Prophylactic, 0·2 to 0·4 g. every four hours, with a max. of 1·2 g. daily. Therapeutic, 0·2 to 0·4 g. every four hours, with a max. of 2·4 g. daily.

Rubiazol is 4'-sulphonamido-2:4-diamino-6-carboxyazobenzene, and differs from Prontosil Rubrum in that the latter does not carry the carboxyl group.

It is used similarly to sulphanilamide.

[P1-81-84] **Rubiazol Injectable** (*Roussel Laboratories, London*) is the disodium salt of 4'-sulphamidophenyl azonaphthol-7-acetyl-amino-3, 6-disulphonic acid, issued in 5 ml. ampoules of a 5% solution for intramuscular injection.

[P1-81-84] **Sulphapyridinum**. *Syn. and Prop. Name*. 2-SULPHANILYL-AMINOPYRIDINE, N<sup>2</sup>-SULFANILYL-2-AMINOPYRIDINE, DAGE-NAN (M & B 693) (*Pharmaceutical Specialities (May & Baker) Ltd., London*).  $\text{NH}_2\cdot\text{C}_6\text{H}_4\cdot\text{SO}_2\text{NH}\cdot\text{C}_5\text{H}_4\text{N} = 249\cdot3$ .

*Dose*.—8 to 60 grains (0·5 to 4 g.) orally. Where the drug is badly tolerated by oral administration, or where there is difficulty in employing it by this route, it may be given by intramuscular injection. For this purpose it is supplied in ampoules containing an oil suspension of 0·5 g., or the sodium salt may be employed (*see Sulphapyridinum Solubile*). For fuller details as to dosage in individual diseases see the section on USES.

Sulphapyridine is 2-(*p*-aminobenzenesulphonamido)-pyridine, and consists of a white, odourless, practically tasteless, crystalline substance. M.p. 190° to 193°.

**Introduction.** The success achieved by sulphanilamide as a chemotherapeutic agent stimulated the search for substances of similar basic structure capable of widening the comparatively limited field of usefulness of this class of drug. Sulphapyridine, synthesised by A. J. Ewins and M. A. Phillips in 1938, was the



first big advance in this direction, possessing, as it does, notable powers in combating the effects of pneumococci, organisms hitherto outside the effective province of the sulphonamides.

**Soluble** about 1 in 3000 of cold water, and about 1 in 100 of boiling water; soluble about 1 in 400 of alcohol 95%; also soluble in acetone. With strong bases or mineral acids it forms water-soluble salts.

**Toxic Effects.** The toxic effects resulting from the use of sulphapyridine are essentially the same as those described under sulphanilamide, though, in general, they do not occur with such frequency. Nausea and vomiting, however, are much commoner with sulphapyridine and are sometimes very severe; at the same time, the use of the drug should not necessarily be discontinued because of vomiting, which often occurs early in the treatment and may cease later. Cyanosis is usually less marked than with sulphanilamide, and sulphæmoglobinæmia is of rare occurrence. Generally, it may be said that patients on high dosage of sulphanilamide look ill, owing to cyanosis, and those on sulphapyridine feel ill, owing to depression and nausea.

Drug fever and dermatitis are less frequent, though, as with sulphanilamide, patients undergoing treatment should avoid exposure to sunshine or ultra-violet light.

Acute hæmolytic anæmia may occur in the first few days of treatment, and severe leucopenia, or even granulocytopenia, is not uncommon; some fatal cases of agranulocytosis have been recorded. As with sulphanilamide, it is important, in the case of prolonged treatment, to keep a watch on the blood picture, especially from the point of view of the white cell count.

Several instances of hæmaturia have been reported as a result of sulphapyridine therapy; the condition appears to be more likely to arise in children, and may be more common in warm climates. It is thought probable that the condition is associated with the formation in the renal tubules and pelvis of calculi consisting largely of acetylsulphapyridine, which occurs in sharp needles, causing damage to the renal tissues. In order to avoid this toxic manifestation, it is important to administer enough fluids during treatment to keep the patient's urinary output at or above the normal level, in order to lessen the chances of calculus formation.

As with sulphanilamide, the use of sulphur-containing foods and of saline purgatives should be avoided during treatment, as also the use of phenacetin, amidopyrine, gold salts, and organic arsenical preparations.

High dosage with sulphapyridine should be avoided in the presence of impaired renal function.

It has about one-fourth of the toxicity of sulphanilamide for rats and mice. It appears to have no effect in relatively large doses on blood, urine and general health, and caused no significant inhibition of growth. It does not produce porphyrinuria.—R. Wien, *Quart. J. Pharm.*, 1938, 217.

Severe skin and general reaction, following the administration of sulphapyridine and exposure to ultra-violet light. Patients should be expressly warned

of the danger of exposure to strong sunlight, or any form of artificial sunlight, while taking this treatment.—R. Hallam, *Brit. med. J.*, i/1939, 559.

It is suggested that the routine employment of methylene blue, in conditions calling for the prolonged administration of sulphapyridine, may be a useful measure in preventing cyanosis, though it has no effect in preventing or modifying the cyanosis of sulphæmoglobinæmia.—D. Campbell and T. N. Morgan, *Lancet*, ii/1939, 123.

Five cases of hæmaturia associated with its use in children, with one death. Children are probably more susceptible to renal complication in sulphapyridine medication, and more care should be taken during its administration in pediatric cases.—Y. F. Tsao, *J. Amer. med. Ass.*, ii/1939, 1316.

A case of agranulocytic angina, following administration in typhoid fever. Though apparently less toxic than sulphanilamide, it is still in certain circumstances not without danger to the leucopoietic system.—R. V. Coxon and J. R. Forbes, *Lancet*, ii/1938, 1412.

Agranulocytosis, following administration. Frequent blood examinations should be made on all cases where sulphapyridine is continued for more than a week and large doses are given.—M. E. Sutherland, *Lancet*, i/1939, 1208.

Agranulocytosis, following the use of sulphapyridine in pneumonia. Recovery.—B. Pringle *et al.*, *Brit. med. J.*, i/1940, 212.

Two patients had renal calculi after sulphapyridine treatment; one had had only 11 g. of the drug and the other 555 g. Both patients had hæmaturia and one had also renal colic. Hæmaturia and other renal symptoms, after sulphapyridine administration, are caused by the deposition of sulphapyridine crystals and concretions in the kidneys and ureters. Frequent examinations of the urine, particularly for red blood cells, should be made during treatment, and the drug should be withheld or used cautiously if hæmaturia occurs, or if there is a diminished kidney function.—N. Plummer and F. McLellan, *J. Amer. med. Ass.*, i/1940, 943.

**Pharmacology.** The absorption of sulphapyridine from the gastro-intestinal tract is slower, less complete, and more variable than is that of sulphanilamide under the same conditions. The differences in absorption seem to be due to an individual response on the part of the patient. There are indications that with excessive dosage there is incomplete absorption.

Sulphapyridine resembles sulphanilamide in its ready penetration of all tissues and body fluids in a concentration not far removed from that of the blood, but unlike sulphanilamide it is usually present in higher concentration in the liver than in other tissues. The mode of excretion appears to resemble very closely that of sulphanilamide, though it is somewhat slower.

The mechanism of action of sulphapyridine is still in doubt. The most commonly accepted theory at present is that, like sulphanilamide, it hinders the growth and multiplication of sensitive bacteria, and thus assists the natural defensive mechanism of the body in destroying the invading organisms.

**Uses.** In general it may be said that whereas the outstanding characteristic of sulphanilamide from the clinical aspect is its effectiveness in the treatment of streptococcal infections, that of sulphapyridine is in the treatment of pneumococcal infections. Its value in pneumonia is now so well established as to be beyond question.

In addition to its striking successes in pneumococcal infections, however, it has also proved remarkably effective in infections due to gonococci and meningococci. In gonorrhœa it is stated to give at least as high a percentage of cures as sulphanilamide, with the

added advantage that the recommended period of delay in starting treatment with the latter drug is not considered necessary in the case of sulphapyridine. Other gonococcal infections in which sulphapyridine has been used with success include gonococcal ophthalmia, gonococcal urethritis, and gonococcal vulvo-vaginitis.

In the treatment of meningococcal meningitis it has now, in large measure, supplanted sulphanilamide, in spite of the latter's undoubted efficacy. It has one important advantage in comparison with sulphanilamide, namely, that it is not only as effective as the latter in the treatment of meningococcal meningitis, but is unique in its action on pneumococcal meningitis.

Other conditions which have responded well to sulphapyridine include chancroid, lymphogranuloma inguinale, granuloma venereum, trachoma, and typhoid. Although it is claimed to be effective in the treatment of *B. coli* infections of the urinary tract, it has not been so widely employed in this connection as sulphanilamide.

While it is not generally advocated in the treatment of staphylococcal infections, it has been used with good results in a few cases of staphylococcal urethritis and staphylococcal septicaemia.

### References to the More Important Uses of Sulphapyridine

The remarks appearing under this heading in respect of sulphanilamide are equally applicable to sulphapyridine. Here again, the more important indications have been prefaced by a summary, giving details as to dosage and technique of administration.

**GONORRHOEA.** Sulphapyridine exerts its curative action at a very early stage in the disease. It is not, like sulphanilamide, dependent for its maximum effect on the development of specific immunity. In order to maintain a therapeutically effective concentration of the drug in the body fluids, it should be administered at four-hourly intervals throughout the day, the last dose being given at bedtime. Nausea and vomiting may be minimised or avoided by the concurrent administration of 5 gr. of sodium bicarbonate.

There is considerable variation among clinicians in the matter of dosage and length of administration; some favour an intensive dosage over a short period of three or four days, others a low dosage continued for two or three weeks. A more common practice is to use a moderate dosage, giving 4 g. on the first day, and continuing with 3 g. daily until from 15 to 20 g. have been given, and thereafter terminating administration altogether, or continuing with a daily dosage of 1.5 to 2 g. for a further week.

On the concurrent use of urethral irrigation (e.g., with 1 in 8000 potassium permanganate solution) opinion is still divided; it is strongly advised by some authors, while others consider it unnecessary or even undesirable.

On the other hand, the concurrent use of vaccines for the purpose of raising the patient's immunity is generally regarded as unnecessary with sulphapyridine, except perhaps in the

comparatively few cases which do not show a marked clinical response within the first five days of treatment.

In women the dosage of the drug is usually lower than in men, 2 g. daily being the customary amount advised.

In all cases, after apparent clinical cure has taken place, the patient should abstain from alcohol and from coitus for three or four weeks, and should be kept under observation for at least three months after all signs and symptoms have subsided.

From a series of 250 cases it is concluded that the results of treatment of acute gonorrhœa in male out-patients with sulphapyridine (either orally or by injection) are superior to those obtained with sulphanilamide or other sulphonamide drugs. The employment of the compound immediately upon diagnosis leads to the rapid cessation of the symptoms and the almost complete absence of complications due to the extension of the disease. An important property of sulphapyridine is that there is no necessity (as with sulphanilamide) to consider any delay in the commencement of the treatment to allow of antibody formation.—V. E. Lloyd, D. Erskine and A. G. Johnson, *Lancet*, ii/1938, 1160; see also E. E. Prebble, *ibid.*, 1163.

The most potent anti-gonococcal agent available at present (report on 102 cases). It can effect clinical cure within a week in the large majority of cases whether of short or long duration, and whether occurring in men or women. No irrigation or other adjuvant treatments are necessary. Toxic effects occur in less than one-third of the cases, but they are usually mild and require only a reduction of the dose. Vulvovaginitis also responds well.—R. C. L. Batchelor *et al.*, *Brit. med. J.*, i/1938, 1142.

Sulphapyridine (19 g. in seven days) was used in the treatment of 100 cases of acute gonorrhœa in males. Lavage of the anterior urethra with potassium permanganate for three weeks was also given. Delay in starting treatment is unnecessary and undesirable. The daily urethral smear did not show the granularity and loss of definition shown with sulphanilamide, but often the gonococci disappeared within 24 hours. Urethral discharge disappeared in 4-5 days on an average. About 45% of the patients complained of toxic effects, though these were less than those of sulphanilamide. Similar results were obtained with 101 cases at another Glasgow clinic.—J. G. McGregor-Robertson, *Lancet*, ii/1938, 1463.

The most effective therapeutic agent yet introduced in the treatment of gonorrhœa, but in face of failure to respond within a week, or of early relapse, persistence with sulphapyridine, even in repeated doses, has proved ineffective. In such circumstances resort should be made to some other form of therapy.—F. J. T. Bowie *et al.*, *Brit. med. J.*, i/1939, 711.

A very high percentage of cures can readily be obtained provided the drug is not withdrawn too early. A satisfactory scheme of dosage appears to be 3 g. daily for one week, followed by 1.5 g. daily for a further week. Patients appear to improve more satisfactorily when irrigations are used in addition. Cures can be obtained in 92.5% of early acute cases and in 82.1% of chronic cases in all grades of severity.—E. E. Prebble, *Brit. med. J.*, i/1940, 89.

Sulphanilamide and sulphapyridine are both potent drugs in the treatment of gonorrhœa, and give approximately the same percentage cure. Sulphapyridine is much easier to use, with a lower incidence of drug resistance and complications of gonorrhœa. There is a high rate of defaulters with both drugs.—R. C. L. Batchelor, *Brit. med. J.*, i/1940, 961.

**MENINGOCOCCAL MENINGITIS.** In this condition sulphapyridine is now universally recognised as the drug of choice, the two essentials for successful treatment being early administration and adequate dosage. Directly a clinical diagnosis is made, sulphapyridine therapy should be commenced without waiting for bacteriological confirmation, and without delaying until the patient has been admitted to hospital. The aim should be to maintain in the cerebrospinal fluid a concentration of the drug equal to 5 mg. per 100 ml. for three days, and a diminishing concentration for a

further five or six days. Large dosage in the first 48 hours is the most important factor.

The following scheme of dosage is recommended in the "Memorandum on Cerebro-spinal Fever" issued by the Ministry of Health in March, 1940 (*H.M.S.O. Memo. 234/Med.*). During the first  $2\frac{1}{2}$  to 3 days the daily dosage is: for infants under 2 years, 3 g.; from two to five years,  $4\frac{1}{2}$  g.; from five to ten years, 6 g.; from ten to fifteen years,  $7\frac{1}{2}$  g.; fifteen years and over, 9 g. The drug should be given four-hourly night and day during the first few days and thereafter, if considered desirable, six-hourly. In adults, at the commencement of treatment, the first two single doses may be increased to a maximum of 2 g. each; thereafter the four-hourly doses should not exceed  $1\frac{1}{2}$  g. each, or a total twentyfour-hour dose of 9 g. After the first  $2\frac{1}{2}$  to 3 days the dose should be gradually reduced over the next four to five days, and the treatment should be completed in from 7 to 9 days. (This dosage scheme is applicable either to sulphanilamide or to sulphapyridine, though there is evidence that a somewhat lower dosage of sulphapyridine will often be successful.)

The drug is best given by the oral route, and if a dose is vomited, it should be repeated (*e.g.*, in a suspension of mucilage of tragacanth). If vomiting continues it is a good plan to change to sulphanilamide. Alternatively, the drug may be given through a nasal or stomach tube, or sulphapyridine soluble may be given by deep intramuscular injection. From the commencement of treatment it is imperative to administer large quantities of fluids (3 to 4 pints daily). After an initial lumbar puncture for diagnosis, further puncture should not be done except to relieve pressure symptoms, and on alternate days to verify the effective action of chemotherapy. (Recommendations as to dosage and technique of administration, on similar lines to the foregoing, have also been issued by the War Office.)

It may be added that sulphapyridine has proved so successful in the treatment of this condition that the use of serum is now generally considered unnecessary, even as an adjuvant.

Proved a successful chemotherapeutic agent in the treatment of six cases of meningococcal meningitis. The dosage was empirical, but a routine administration was adopted, calculated to produce a high concentration of the drug in the body fluids within a few hours of the inception of treatment, and to maintain this concentration at a steady level. 1 gramme of the drug was given at 0, 2 and 4 hours, and subsequently at intervals of 4 hours; thereafter the dose was reduced as the clinical picture improved, but the interval was maintained. Toxic symptoms were unimportant.—F. J. Hobson and D. H. G. MacQuaide, *Lancet*, ii/1938, 1213.

Three cases of meningococcal cerebrospinal meningitis successfully treated with sulphapyridine (average total dose 29 g.) and daily lumbar puncture.—W. H. Osborn, *Brit. med. J.*, i/1939, 1281.

In 143 consecutive cases treated with sulphapyridine, the case mortality was 10%, compared with a usual case mortality (in the Sudan) of 68 to 80%. R. B. U. Somers, *Lancet*, i/1939, 921.

In a small series of cases (50) it was found that with sulphapyridine the mortality was 7%, whereas with serum or sulphanilamide it was over 60%. There was thus a significant difference between the results obtained with sulphanilamide and with sulphapyridine respectively.—E. A. Underwood, *Brit. med. J.*, i/1940, 757.

The dramatic success of chemotherapy in this disease is one of the high lights of modern medicine. No other infection responds so constantly and so dramatically to high dosage with sulphapyridine and sulphanilamide. The two essential points are early administration and adequate dosage during the first two or three days. As soon as the diagnosis is suspected on clinical grounds, a full dose of sulphapyridine should be given without waiting for confirmation by lumbar puncture.—*Brit. med. J.*, i/1940, 397.

Sulphapyridine appears to be a drug of exceptional therapeutic value in the treatment of cerebrospinal fever, but its value is probably greatest when combined with serum or antitoxin therapy.—J. H. Jordan *et al.*, *Brit. med. J.*, i/1940, 1005.

When adequate doses of sulphapyridine are given the disease can be effectively controlled without therapeutic lumbar puncture. On the first day a maximum total of 10 g. is given (2 g. on admission, 2 g. two-hourly for two doses, and 1 g. four-hourly); on the second day, 1 g. four-hourly; on the third day, 1 g. six-hourly; and thereafter 1 g. eight-hourly, the daily dosage being maintained at 3 g. until a total of 30 g. has been given, when a differential white count is taken. If all signs of meningeal irritation have not disappeared by then, and if the number and type of polymorphonuclear leucocytes are satisfactory, treatment is continued until the last trace of neck rigidity has disappeared.—D. Williams and D. Brinton, *Lancet*, ii/1940, 482.

**PNEUMONIA.** The early good reports as to the action of sulphapyridine in pneumonia have been fully confirmed by subsequent workers. According to Marriott (*Brit. med. J.*, ii/1939, 944), the principal points now established concerning the sulphapyridine treatment of lobar pneumonia are: (1) Average reduction in gross mortality is such that three patients out of four who would formerly have died may now live. (2) It is particularly valuable in severe cases with bacteraemia. (3) It is as effective in the elderly as in the young. (4) It is effective against pneumococci of all types. (5) Temperature falls by rapid lysis within 24 to 36 hours of sulphapyridine being started, irrespective of the day of the disease, and there is usually remarkable improvement in the general condition with uneventful recovery in most cases. (6) The incidence of empyema appears lessened, but clear pleural effusions are commoner. (7) Specific agglutinins against pneumococci develop within the fifth and twelfth day of the disease, as they do in untreated cases.

The dosage is determined by the severity of the infection, with the proviso that a high concentration (4 or 5 mg. per 100 ml.) of the drug be obtained in the blood stream as rapidly as possible by the administration of relatively large doses at frequent intervals. Severely ill patients, or those in whom the disease is well established, should be given 2 g. as an initial dose, followed by a further 2 g. in four hours, and then 1 g. four-hourly for 36 hours, except during sleep. Clinical improvement will generally be evident by this time, and the dosage may then be reduced to 0.5 g. four-hourly for another 24 or 36 hours, and then to 0.5 g. eight-hourly for two days, a total dosage of 20 g. being usually sufficient. In less severe cases, after an initial dose of 2 g. four-hourly, administration of 1 g. may be commenced. The drug is well tolerated by children, and the following dosages have been suggested both for lobar pneumonia and broncho-pneumonia: from 1 to 3 months, 0.125 g.; from six months to two years, 0.25 g.; at three years, 0.375 g.; and at five years, 0.5 g.; all doses given four-hourly. In severe

cases an initial double dose may be given if necessary, followed by the usual dose four-hourly until the temperature has become normal, after which a smaller dose should be given eight-hourly for two more days.

Treatment should always be continued for two days after the positive fall of temperature, as otherwise there may be a recurrence of the pneumonic process.

It is still open to question whether a type-specific serum should be used in addition to sulphapyridine, and there is a considerable body of evidence to show that the combination of the two may give better results. Administration of sulphapyridine should not, however, be allowed to wait on the typing of the pneumococci.

It should be noted that simultaneous administration of cough mixtures, other than simple linctus, is undesirable during sulphapyridine therapy.

In 100 cases of lobar pneumonia treated with sulphapyridine, the case mortality rate was 8%, compared with 27% in a control series observed at the same time.—G. M. Evans and N. F. Gaisford, *Lancet*, ii/1938, 14.

In every one of eight cases of lobar pneumonia, exhibition of the drug was followed by immediate fall of temperature and pulse-rate, and by improvement in the clinical condition, with subsequent uneventful course and rapid recovery. Serum and other forms of treatment were withheld. A suitable dose for the commencement of treatment in an adult appears to be 4 tablets (2 g.), followed by two tablets four-hourly for 20 hours, and thereafter by the same dose six-hourly. Administration of the drug should last at least 5 days, no matter how favourable the clinical condition. Children tolerate the drug well.—S. C. Dyke and G. C. K. Reid, *Lancet*, ii/1938, 1157.

In 50 cases treated by non-specific treatment there were 8 deaths, as compared with one death in 50 cases treated by sulphapyridine. The course of the disease was considerably modified by the drug, and the pyrexial period was reduced.—T. F. Anderson and R. M. Dowdeswell, *Lancet*, i/1939, 252.

A very effective and convenient drug in the treatment of pneumonia.—A. L. Agranat *et al.*, *Lancet*, i/1939, 309, 380.

Gave good results in the treatment of pneumococcal infections in infants and children.—H. L. Barnett *et al.*, *J. Amer. med. Ass.*, i/1939, 578.

An effective drug in the treatment of pneumonia. Report of 100 cases. A conspicuous effect is its ability to bring about, within 24 to 48 hours, a critical drop in temperature, followed by prompt clinical improvement.—H. F. Flippin *et al.*, *J. Amer. med. Ass.*, i/1939, 529.

Sulphapyridine therapy was carried out in 50 cases of pneumonia, with a mortality rate of 6%, as compared with mortality rates of 23% in a series of 30 control cases, and 12% in a series of 50 cases treated with specific anti-pneumococcus serum.—D. Graham *et al.*, *Canad. med. Ass. J.*, i/1939, 332.

A single dose of pneumococcus vaccine given to mice or rabbits profoundly affects the course of an experimental infection in these animals when treated with sulphapyridine, and a strong case is made out for the combined use of vaccine and sulphapyridine in all cases of pneumonia in man. Pneumococci in an infected animal treated with sulphapyridine, readily established a tolerance or fastness to the drug; thus, it is essential that the initial doses should be large and that the immunity should be raised to as high a degree as possible by any means, so that the destruction of the bacteria may be complete before they have established tolerance to the drug.—J. H. Maclean, K. B. Rogers and A. Fleming, *Lancet*, i/1939, 562.

Acquired tolerance of pneumococcus to sulphapyridine in the human being. It is desirable to increase the immunity at the same time that sulphapyridine is administered, so that if possible the infecting cocci can be destroyed before they have had time to acquire a tolerance to the drug.—R. W. Ross, *Lancet*, i/1939, 1207.

There is a good case for the use of pneumococcal vaccines in pneumonia in man in conjunction with sulphapyridine. If possible, the pneumococcus should be typed and a vaccine of the specific type administered, but if typing is not

possible, then a stock polyvalent vaccine can be administered at once, and the sooner the better.—A. Fleming, *Brit. med. J.*, ii/1939, 104.

Observations on 342 cases. The average dose administered to 284 patients of more than 10 years of age was 22 g. Excluding fatal cases, a rapid effect was produced in all cases except 5. The commonest complications were pleural effusion (18 cases) and otitis (9 cases).—O. Romcke and E. Vogt, *Lancet*, ii/1939, 778.

The excellent results in lobar pneumonia are paralleled in the less clearly defined pneumococcal chest infections, and results in bronchitis, broncho-pneumonia and post-operative pneumonia are good.—H. L. Marriott, *Brit. med. J.*, ii/1939, 944.

Of considerable value in type II pneumococcus pneumonia. It has three disadvantages: (1) the definite lag in recovery, (2) the delay in resolution of the consolidation, (3) the gastric upset which sometimes necessitates stoppage of treatment.—T. Anderson *et al.*, *Lancet*, ii/1939, 776.

A series of 234 cases were treated, of whom 78 were controls (conservative treatment) with 21 deaths. 119 were treated with sulphapyridine alone, giving a case mortality of 6.7%; and 37 cases of either type I or type II treated with sulphapyridine, plus specific serum, with 3 deaths.—C. S. D. Don *et al.*, *Lancet*, i/1940, 311.

The best routine method of starting treatment is to give 4 tablets, *i.e.*, 2 g., immediately, and repeat at 4-hourly intervals for three or, in severe cases, 4 doses, and then to continue with 2 tablets 4-hourly till the temperature falls, following with a further one tablet 8-hourly for three doses. Giving a patient one tablet two or three times a day cannot be expected to modify the course of the disease appreciably, and certainly not to cause a fall of temperature in 24 hours.—W. F. Gamford, *Practitioner*, i/1940, 38.

An analysis of the clinical results of treatment with serum and sulphapyridine suggests that the combination of the two represents the optimum therapy in pneumococcal infections. The cases in which the combined therapy was most effective were bacteremic patients, particularly those over 50, those in whom treatment was started late in the disease, and the ones with blood cultures that yielded moderate or large number of pneumococci; patients in whom more than one lung was involved; most patients over 60 who had more than a mild infection; and pneumonias due to types II and III, and possibly V pneumococci, except the mild cases.—M. Finland *et al.*, *New Engl. J. Med.*, i/1940, 739.

Fourteen patients suffering from pneumococcal pneumonia, and who did not appear too ill on admission, were treated by *rectal* administration of sulphapyridine alone, and all recovered. The sulphapyridine was initially administered in 6 g. doses suspended in 3 ounces of water, with from 0.66 to 1 g. of sodium bicarbonate. After a cleansing enema this suspension was introduced as a retention enema. At 4-hourly intervals, 2 g. doses, and later 3 g. doses, were employed. It was found that three times the usual oral dose was required to produce adequate blood levels. The clinical response was slower than with the oral route, but was uniformly satisfactory. The average time required for the temperature to reach normal was 48 hours, as compared with 36 hours in those treated orally, and 12 hours in those treated intravenously. The same decrease in toxicity was also noted. Only one patient exhibited nausea and vomiting, and there was no evidence of rectal irritation. The rectal method is satisfactory and less disturbing for patients showing gastric irritability and not too seriously ill.—W. L. Whittemore *et al.*, *J. Amer. med. Ass.*, i/1940, 940.

#### Miscellaneous References

**BACTERIAL ENDOCARDITIS.** A case recorded of recovery, following administration of sulphapyridine. Three courses were given, using the oral method of administration for the first two, and the intramuscular route for the third. In the first course the patient had 12 g. in 5 days, in the second 6 g. in 2 days, and in the third 2 g. intramuscularly.—C. T. Andrews, *Brit. med. J.*, i/1940, 5.

**CHANCROID.** Treatment with sulphanilamide or sulphapyridine cures rapidly; a daily dose of 2 to 3 g. of the latter for 5 to 10 days is sufficient to produce a cure. Intravenous injections of Dmelcos vaccine may also be used, but this causes severe systemic upset.—Robert Lees, *Med. Pr.*, 1939, 615.

Complete healing in 45 cases in two weeks, with no recurrence in the next six months.—Kornblith, Jacoby and Wishengrad, *J. Amer. med. Ass.*, ii/1938, 523.

**GONOCOCCAL OPHTHALMIA.** Rapid cure of two cases.—A. M. Michie and M. H. Webster, *Lancet*, ii/1938, 373.



**GONOCOCCAL URETHRITIS.** Is undoubtedly superior to Prontosil Album and Uleron in the treatment of acute gonococcal urethritis in the male sex.—R. Marinkovitch, *Brit. med. J.*, i/1939, 317.

**GONOCOCCAL VULVOVAGINITIS.** The advantages of sulphapyridine over sulphanilamide are shown in the shorter duration of drug treatment and omission of local treatment to the urethra, vagina and rectum.—D. K. Brown, *Brit. med. J.*, i/1939, 321.

In this condition, occurring in little girls, sulphapyridine is of outstanding value. To effect the resolution of the acute inflammatory state in a few days, and to be able to dispense with the repeated daily local treatment in these children, is one of the major triumphs of modern chemotherapy.—V. E. Lloyd, *Practitioner*, i/1940, 49.

**LYMPHOGRANULOMA INGUINALE.** Uniformly successful in 12 cases treated with 5 to 6 0·5 g. tablets daily for 5 days, followed by an interval of 3 or 4 days and the course repeated.—K. V. Earle, *Lancet*, ii/1939, 1265.

**PEMPHIGUS NEONATORUM.** A case successfully treated in a child of two weeks.—A. J. Troup and R. M. White, *Lancet*, ii/1939, 1367.

**PNEUMOCOCCAL MENINGITIS.** Recovery in a girl of 7.—G. C. K. Reid and S. C. Dyke, *Lancet*, ii/1938, 619.

**PNEUMOCOCCAL SEPTICÆMIA.** Prompt subsidence of symptoms, following use in a woman of 61.—S. C. Dyke, *Lancet*, ii/1938, 621.

**STAPHYLOCOCCAL SEPTICÆMIA.** A case successfully treated.—W. J. Fenton and F. Hodgkiss, *Lancet*, ii/1938, 667.

A case successfully treated.—E. J. O'Brien and C. J. McCarthy, *Lancet*, ii/1938, 1232. A second case.—J. Maxwell, *ibid.*, 1233.

**TRACHOMA.** Remarkable remissions of pathologic signs obtained in two cases of chronic trachoma, intractable to all other methods of treatment, and vision improved greatly in both cases. Sulphapyridine was prescribed 7½ gr. every 4 hours.—M. D. Spearman, *J. Amer. med. Ass.*, ii/1939, 1807.

Remarkable results may be expected from this treatment in many cases of bacterial conjunctivitis and blepharitis, especially when associated with trachoma.—A. F. MacCallan, *Brit. med. J.*, i/1940, 482.

**TUBERCULOSIS.** Sulphapyridine has a beneficial effect on certain cases of pulmonary tuberculosis. It inhibits the growth of pneumococci in the distressed areas and relieves unpleasant symptoms—malaise, night sweats, etc. Commence with one tablet (0·5 g.) four times a day after food for three days; then reduce to one tablet night and morning and later to one tablet daily.—J. Deeny, *Brit. med. J.*, i/1939, 696.

**TYPHOID.** 7 cases successfully treated.—E. H. R. Harries *et al.*, *Lancet* i/1939, 1321.

#### [P1·S1·84] Sulphapyridinum Solubile.

**Prop. Name.** DAGENAN-SODIUM (M & B 693 SOLUBLE) (*Pharmaceutical Specialities (May & Baker) Ltd., London*).

$\text{NH}_2\cdot\text{C}_6\text{H}_4\cdot\text{SO}_2\text{N}(\text{Na})\cdot\text{C}_6\text{H}_4\text{N}\cdot\text{H}_2\text{O} = 289\cdot3$ .

**Dose.**—Soluble sulphapyridine is supplied in ampoules containing 1 g. in 3 ml. of solvent for intramuscular injection. It should be used only when oral therapy is impracticable, and the general directions as to dosage given under sulphapyridine should be followed, but it is advisable that not more than 4 to 6 injections should be given consecutively. The oral route of administration should be resumed as soon as possible. The salt has also been employed intravenously (*vide infra*):

The mono-hydrated sodium salt of sulphapyridine, occurring as a white, odourless, crystalline powder, melting with decomposition at 316·5° to 317°.

**Soluble** about 1 in 1·6 of water at 25°, the pH of a 1% solution being 10·4; slightly soluble in organic solvents.

Owing to its high alkalinity, intramuscular injection of this drug is apt to be painful and may even cause sloughing, while intravenous injection needs to be frequently repeated in order to maintain an adequate blood level. On the other hand, sulphapyridine itself dissolves to a greater extent in normal saline than in water, and to a still greater extent in a glucose solution. The largest amount dissolved in a series of experiments employing different solvents was 0.279 g. per 100 ml. in 0.85% saline, also containing 5% glucose. It is therefore possible to reduce by half the volume in which sulphapyridine must be contained if given by injection. 43 cases have been treated by this method, dissolving a standard dose of 2 g. of sulphapyridine in 1 litre of glucose-saline. Immediate effect can be secured by injecting the first dose intravenously, succeeding doses being given subcutaneously at 8 hour, and later at 12 hour, intervals. Satisfactory blood levels are maintained and the solution causes no local damage.—J. W. Haviland and F. G. Blake, *Amer. J. med. Sci.*, 1940, 199, 385.

**Painless injection.** A 1 ml. Record syringe, with a No. 2 serum needle, is filled with 1% Novocain; a weal is made intradermally and the needle is driven through this, injecting a little Novocain as it goes, until the needle is in the muscle, when 0.5 ml. of Novocain is injected. The syringe is then detached from the needle which is left in place. A 5 ml. Record syringe with a large needle is used for the sulphapyridine. The syringe is detached from the filling needle and attached to the needle in the patient and the drug injected. The empty 5 ml. syringe is detached from the needle and the former 1 ml. syringe containing about 0.5 ml. of 1% Novocain is re-attached. About 0.25 ml. of Novocain is injected to clear the needle, which is then withdrawn while the rest of the Novocain is injected into the track to prevent any of the sulphapyridine escaping up the track after the needle has been withdrawn. If this technique is followed the intense pain usually experienced by patients is entirely avoided.—H. J. McCurrich, *Brit. med. J.*, ii/1939, 1205.

**PNEUMONIA.** Clinically, it is no more toxic than sulphapyridine, is rapidly absorbed and excreted, and is less likely to cause vomiting than sulphapyridine given orally. It is best given intramuscularly—4 to 6 injections of 3 ml. at 4-hourly intervals, which may be followed by smaller doses (1 g. four-hourly) of sulphapyridine orally, till the temperature falls.—W. F. Gaisford *et al.*, *Lancet*, ii/1939, 69.

For **intravenous injection** 2 g. of soluble sulphapyridine in 20 ml. of normal saline may be adopted as the standard initial dose, and this dose may be repeated in 4 to 6 hours. In 14 out of 18 cases the therapeutic effect was rapid, occurring within 6 to 12 hours. There was no local or systemic reaction and nausea occurred in only one case. The chief difficulty was in maintaining constant blood levels, with a consequent erratic course of recovery. In seriously ill patients it is desirable to give soluble sulphapyridine intravenously at first, and follow it immediately with sulphapyridine orally.—W. L. Whittmore *et al.*, *J. Amer. med. Ass.*, i/1940, 940.

Intravenous injections of a 5% solution of soluble sulphapyridine were given to 30 patients suffering from pneumococcal lobar pneumonia, a standard dose of 3.8 g. being adopted for adult patients. No untoward symptoms were noted, except vomiting during or immediately after the injection. The intravenous use is advantageous in that blood levels of from 5 to 8 mg. per 100 ml. can be attained with great speed and certainty, but it should be limited to cases in which oral administration is impossible, or does not suffice for successful therapy. Injections should be given slowly, at the rate of 5 ml. of the solution per minute, and care should be taken that none of the solution gets outside the vein, or a bad slough may result, since the solution is alkaline. This dose may be repeated at intervals of six to eight hours, though it is seldom necessary to give more than two injections. Sulphapyridine in doses of 1 g. every four hours should be started at the time of intravenous therapy. It is also employed in the treatment of patients with pneumonia not responding to therapy by the mouth. If on the day following sulphapyridine therapy by the mouth, the patient's temperature is not below 101°F. rectal, and the concentration of free sulphapyridine in the blood is below 4 mg. per 100 ml., a single dose of 0.06 g. of the sodium salt per Kg. of body-weight in 5% solution is given intravenously, and this results in a prompt return of temperature to normal.—E. K. Marshall and P. H. Long, *J. Amer. med. Ass.*, i/1939, 1671.

Successfully employed by **hypodermoclysis** in more than 50 cases of pneumonia and other conditions in which sulphapyridine was indicated, but in

which oral administration was difficult or impossible. The drug was given in from 0.3 to 0.7% solution in normal saline, the usual dose being 3 to 7 g. in one litre, repeated in 24 to 36 hours as the condition required, and injected into the thighs or under the breasts at the rate of from 200 to 300 ml. an hour. No local reactions were observed.—G. V. Taplin *et al.*, *J. Amer. med. Ass.*, i/1940, 1733.

**PNEUMOCOCCAL MENINGITIS.** A case of pneumococcal meningitis successfully treated by soluble sulphapyridine (previous fatality-rate in 39 cases 100%).—J. V. Cable, *Lancet*, ii/1939, 73.

The sodium salt is particularly valuable, and may be given in doses of 3 ml. four-hourly for from four to eight doses. After the intramuscular course is finished, oral treatment may be continued with two tablets four-hourly till the temperature is settled.—W. F. Gaisford, *Practitioner*, i/1940, 41.

[P1·S1·S4] **Sulphathiazolum.** *Prop. Names.* CIBA 3714 (*Ciba, Horsham*), THIAZAMIDE (M & B 760) (*Pharmaceutical Specialities (May & Baker) Ltd., London*).

$\text{NH}_2 \cdot \text{C}_6\text{H}_4 \cdot \text{SO}_2 \text{NH} \cdot \text{C}_3\text{H}_2\text{NS} = 255.3$ .

*Dose.*—15 to 60 grains (1 to 4 g.) (For further details as to dosage in individual diseases, see abstracts under USES.)

Sulphathiazole is 2-(*p*-aminobenzenesulphonamido)-thiazole, occurring as a white, crystalline powder, melting at 202°. It dissolves in mineral acids, forming crystalline salts which are slightly soluble in water, to give strongly acid solutions. The sodium salt, formed by substitution in the remaining hydrogen atom of the sulphonamide group, is a crystalline substance which is readily soluble in water, a 2% solution having a reaction of pH 9.6. It is used for the intramuscular injection of sulphathiazole.

**Soluble** about 1 in 2500 of water, about 1 in 200 of alcohol, and readily in hot acetone.

**Sterilisation.** Sulphathiazole solid heated at 150° for one hour is oxidised, with the formation of a purple colour. To sterilise, it should, therefore, be mixed with about 1% of water and autoclaved in a glass container at 115 lbs. pressure for thirty minutes. Solutions are stable to heat if alkaline and only slightly hydrolysed if acid.

**Toxic Effects.** These are similar to those encountered with the other sulphonamides, though there would appear to be some variation in the incidence. Thus, it is generally agreed that nausea, vomiting, mental depression and cyanosis are markedly less with sulphathiazole than with sulphanilamide or sulphapyridine, whereas drug fever and skin rashes (especially of the nodular type) are of more frequent occurrence. Hæmaturia may occur, but the incidence is lower than with sulphapyridine. There have so far been no reports of acute hæmolytic anæmia or agranulocytosis, though the possibility of their occurrence is not ruled out. On the other hand, a few cases have been observed of injection of the sclera and conjunctiva, a toxic effect which would appear to be peculiar to sulphathiazole. Generally speaking, however, the indications are that sulphathiazole is less toxic than either sulphanilamide or sulphapyridine.

In rapidity of absorption and excretion it resembles sulphanilamide, and in this respect it has an advantage over sulphapyridine.

A further advantage which it possesses over the latter drug is the relatively moderate degree of conjugation to the acetyl derivative, and for this reason determination of total sulphathiazole blood concentrations is not so necessary, knowledge of the concentration of free sulphathiazole being adequate for practical purposes.

One important advantage of sulphathiazole over sulphapyridine is a much less tendency to cause nausea and vomiting; almost equally valuable is the absence of cyanosis. The only organ which appears liable to suffer is the kidney, diminished renal excretion and hæmaturia occurring in some patients, and crystals of the drug being sometimes found in the urine.—*Brit. med. J.*, i/1940, 1022.

Less toxic than sulphanilamide or sulphapyridine.—T. L. Pool and E. N. Cook, *Proc. Mayo Clin.*, i/1940, 113.

These compounds (sulphathiazole and sulphamethylthiazole) seem to produce less nausea and vomiting than sulphapyridine, but drug fever and drug rashes are quite common, and three cases have been observed of congestion of the conjunctiva and sclera with a generalised erythematous eruption; mild hæmaturia has been noted in several cases.—*J. Amer. med. Ass.*, i/1940, 870.

It is evident that sulphathiazole shows certain of the toxic effects described for other therapeutically active sulphonamide compounds. The toxic effects do not seem to offer any serious barrier to its use in treatment, and indeed in many ways toxicity appears to be less than that of sulphapyridine.—J. G. Reinhold *et al.*, *Amer. J. med. Sci.*, 1940, 199, 393.

Compared with sulphapyridine, its use is attended by conspicuously less vomiting, nausea and mental depression; other untoward reactions are less frequent and severe; and the problem of excessive acetylation is not encountered.—F. G. Blake, *New Engl. J. Med.*, ii/1940, 661.

Skin rashes, usually appearing from the fifth to ninth day, are present in 5% of persons treated with sulphathiazole as compared with 1.9% and 2% of those treated with sulphanilamide and sulphapyridine respectively.—Long *et al.*, *J. Amer. med. Ass.*, ii/1940, 364.

It causes less nausea and vomiting than sulphapyridine, but dermatitis occurred more frequently than with sulphanilamide and sulphapyridine.—W. W. Spink and A. E. Hansen, *J. Amer. med. Ass.*, ii/1940, 840.

**Uses.** Early experimental results gave reason to hope that sulphathiazole would prove as effective a therapeutic agent against staphylococci as sulphanilamide had proved against streptococci. Subsequent clinical trials would, however, seem to indicate that its value in this connection is not likely to be so great as was at first anticipated, possibly due to the difficulty in maintaining a sufficiently high blood concentration owing to the rapid absorption and elimination of the drug. On the other hand, from the few clinical trials conducted to date, there is evidence that it is at least as effective as sulphapyridine in pneumococcal and meningococcal infections, while possessing the advantage of lower toxicity. Good results have also been obtained from its employment in urinary tract infections, especially those associated with the presence of staphylococci and of *Streptococcus faecalis*, two types of urinary infection resistant to other sulphonamide treatment. It has so far not been used to any extent in gonorrhœa, but there is some evidence that the results obtained may be comparable with those of sulphapyridine.

Preliminary report of the Council on Pharmacy and Chemistry of the A.M.A. on sulphathiazole and sulphamethylthiazole. Experience to date leads to the belief that these compounds are about as effective as sulphapyridine in pneumococcal pneumonia in human beings and at least as effective in staphylococcal infections.—*J. Amer. med. Ass.*, i/1940, 870.

**GONORRHOEA.** Employed in 19 cases of acute gonorrhœa in males had a rapid initial therapeutic effect comparable to that of sulphapyridine. Not less than 4 g. daily for five days should be given.—V. E. Lloyd and D. Erskine, *Lancet*, ii/1940, 186.

**MENINGOCOCCAL INFECTION.** H. S. Banks treated 15 cases with sulphathiazole, and was impressed with the rapidity of the clinical improvement and the rapid way in which the cerebrospinal fluid cleared up, both bacteriologically and in respect of the cellular count.—*Brit. med. J.*, i/1940, 1033.

**PNEUMONIA.** Not enough is known yet to set up standards of dosage, but for adults suffering from pneumococcal pneumonia an initial dose of 4 g. of sulphathiazole has been given, followed at 4-hour intervals by doses of 1 g. With this dosage it has been noted that after the first 24 hours of medication the concentrations of sulphathiazole in the blood are frequently much lower than would be expected if sulphapyridine had been used, and in some cases it has been difficult to maintain adequate concentration of the drug, probably owing to its rapid absorption and excretion. In several cases a relapse of the pneumonia has been noted in association with these low concentrations of sulphathiazole.—*J. Amer. med. Ass.*, i/1940, 870.

Of 100 cases treated by sulphathiazole, those recovering promptly by crisis or rapid lysis with uneventful convalescence comprised 55% of the group; in 109 cases treated by sulphapyridine the figure was 55%; the number of cases relapsing were respectively one and four; and the number of deaths four and seven. The incidence of toxic drug reactions, which were relatively minor in severity, occurring in the sulphathiazole group, was about half that in the sulphapyridine group.—F. G. Blake, *New Engl. J. Med.*, ii/1940, 661.

In 33 cases of pneumococcal pneumonia sulphathiazole appeared to be as fully effective a therapeutic agent as sulphapyridine.—W. W. Spink and A. E. Hansen, *J. Amer. med. Ass.*, ii/1940, 840.

From a study of 109 patients with pneumonia, 55 of whom received sulphathiazole and 54 sulphapyridine, it was concluded that sulphathiazole is as efficient as sulphapyridine.—S. C. Wagoner and W. F. Hunting, *J. Amer. med. Ass.*, i/1941, 267.

**STAPHYLOCOCCAL INFECTIONS.** Sulphathiazole has little or no effect when there is a positive blood culture. It may be of value in cases where the septic focus has been removed or in localised lesions such as a carbuncle or cellulitis. All deaths resulting from staphylococcal infection are due to bacteraemia and thus this new remedy is not likely appreciably to lower the high death rate. The following dosage is recommended: a minimum of 2 g. at the start and 2 g. four-hourly until an average amount of 30 g. has been given, but in severe cases 2 g. should be given two-hourly, provided a differential white count is made at the end of the second day.—C. E. B. Butler, *Proc. R. Soc. Med.*, 1940, 33, 673.

In the treatment of severe staphylococcal infections the results so far do not support the optimistic reports from America.—C. E. B. Butler, *Brit. med. J.*, i/1940, 1032.

Neither sulphamethylthiazole nor sulphapyridine given by mouth affected the course of experimental staphylococcal lesions of the skin of mice.—A. Macdonald, *Lancet*, i/1940, 1157.

**STAPHYLOCOCCAL SEPTICÆMIA.** 15 consecutive cases were successfully treated with sulphathiazole.—W. W. Spink and A. E. Hansen, *J. Amer. med. Ass.*, ii/1940, 840.

**URINARY INFECTIONS.** The two compounds sulphathiazole and sulphamethylthiazole have definite bactericidal effect on the organisms found in urinary infection when given in the usual dosage by mouth. They differ from sulphanilamide and sulphapyridine in that they kill off strains of *Str. faecalis*. *Str. faecalis* and *Staph. Aureus* are killed by these drugs in lower concentration in the urine than are the gram-negative bacilli.—H. F. Helmholz, *Proc. Mayo Clin.*, i/1940, 65.

A series of 50 unselected cases treated (35 with sulphamethylthiazole and 15 with sulphathiazole). The usual dosage was 1 g. (of either drug) administered four times daily. In some 65% of the patients sterile urine was produced. In every one of five patients with *Staph. aureus* as the infecting organism the urine became sterile and remained so. Of 7 patients with *Str. faecalis* infection 3 were cured (larger doses might have given better results).—T. L. Pool and E. N. Cook, *Proc. Mayo Clin.*, i/1940, 113.

It is a useful adjunct in the treatment of urinary tract infections, especially those due to staphylococci, *B. proteus*,  $\beta$ -haemolytic streptococci, and *B. coli*.—W. W. Spink and A. E. Hansen, *J. Amer. med. Ass.*, i/1940, 840.

**Sulphathiazole Snuff.** 19 subjects, proved to be nasal carriers of staphylococci, were treated with a snuff consisting of 10 parts by weight of sulphathiazole with 90 parts of magnesium carbonate. The snuff was taken six times a day, 1 g. lasting for three to four days, thus involving the taking of approximately 0.03 g. of sulphathiazole per day. The results were very promising; several subjects showed a great reduction in staphylococci and in some these almost disappeared. It may prove of value as a prophylactic against bacterial infections of the upper respiratory tract.—M. E. Delafield, E. Straker and W. W. C. Topley, *Brit. med. J.*, i, 1941, 145.

[P1-S1-S4] **Sulphamethylthiazolum.** *Syn.* SULPHAMETHIAZOLE.  $\text{NH}_2\cdot\text{C}_6\text{H}_4\cdot\text{SO}_2\cdot\text{NH}\cdot\text{C}_3\text{HNS}\cdot\text{CH}_3 = 269.3$ .

*Dose.*—15 to 30 grains (1 to 2 g.).

Sulphamethylthiazole is 2-(*p*-aminobenzenesulphonamido)-4-methylthiazole, m.p. 237°. It is used similarly to sulphathiazole, but cases of peripheral neuritis have been reported as a result of treatment with this salt.

Sulphamethylthiazole experimentally appears to be more effective against *Staph. aureus* than sulphathiazole. There is also preliminary evidence that individuals may receive these preparations without experiencing some of the toxic manifestations of sulphanilamide and sulphapyridine. One patient who had lobar pneumonia, in which there was a mixed infection and in which no definite typing could be obtained, responded to sulphamethylthiazole in exactly the same manner as patients ordinarily do following sulphapyridine treatment. The recovery was rather striking in 48 hours, and the patient was treated for five days without a single evidence of gastro-intestinal irritation, whereas she previously had vomited at the onset of her illness without administration of any drug. In addition three cases are mentioned in which *Staph. aureus* was the offending organism and in which sulphamethylthiazole was used with promising clinical results. The dosage employed in the treatment described consists of two initial doses of 2 g. at a four-hourly interval, followed by 1 g. four-hourly, the concentrations of sulphamethylthiazole in the blood being determined by means of a modification of the Marshall test for sulphanilamide.—W. E. Herrell and A. E. Brown, *Proc. Mayo Clin.*, 1939, 753.

**Sulphonamide E.O.S.**  $\text{NH}_2\cdot\text{SO}_3\cdot\text{C}_6\text{H}_4\cdot\text{NH}\cdot\text{CH}(\text{CH}_3)\text{SO}_3\text{Na} = 302.3$ .

The sodium salt of the *N*-ethylsulphonate of sulphanilamide, prepared by heating sulphanilamide with a concentrated aqueous solution of sodium acetaldehyde-bisulphite. It is very soluble in water (solutions up to 40% can be prepared), and is far less toxic than, and largely free from the unpleasant by-effects of, sulphanilamide and other derivatives. It has a desired degree of stability, but is sufficiently readily hydrolysed in the body to exert a strong bactericidal effect. This was proved in trials upon rabbits, previously converted into "carriers" of typhoid and paratyphoid organisms, and also upon albino mice infected with hæmolytic streptococci productive of septicæmia and puerperal fever. Clinical trials have been successful especially in showing a relative freedom of toxicity. For example, young children and infants have shown a high degree of tolerance for the preparation. The relative non-toxicity suggests its use in lighter ailments such as common colds and as a general safe prophylactic.—A. G. Green and M. Coplans, *Chem. & Ind.*, 1940, 793.

**Sulphadiazines.** Two new heterocyclic derivatives of sulphanilamide, 2-sulphanilamidopyrimidine and 2-sulphanilamido-4-methylpyrimidine, which, in preliminary mouse tests, have shown greater chemotherapeutic activity than sulphapyridine or sulphathiazole, are reported. To avoid confusion the name sulphadiazines is suggested for these compounds.—R. O. Roblin *et al.*, *J. Amer. chem. Soc.*, 1940, 2002; see also Feinstone *et al.*, *Johns Hopk. Hosp. Bull.*, 1940, 67, 427.

**Diaminosulphone.**  $\text{NH}_2\cdot\text{C}_6\text{H}_4\cdot\text{SO}_2\cdot\text{C}_6\text{H}_4\cdot\text{NH}_2 = 248.3$ .

Diaminosulphone is 4:4'-diaminodiphenylsulphone and occurs in long, colourless, rectangular plates, m.p. 176°. It is sparingly soluble in cold water, but more soluble in hot water.

It is active in curing streptococcal infections in mice in doses of about one-hundredth of those required with sulphanilamide, but is 25 times as toxic. The

corresponding dinitro compound (dinitro-sulphone) is not so toxic to mice as sulphanilamide, and its antistreptococcal activity in mice is not inferior to that of the latter substance.—G. A. H. Buttle, *Lancet*, i/1937, 1331.

A comparison of the therapeutic activity of sulphanilamide, sulphathiazole and diaminosulphone with the activity of sulphapyridine against pneumococcus infection in mice, on the basis of the Median Survival Blood Concentrations, gave activity ratios of 0.43, 1.21 and 6.86 respectively.—J. T. Litchfield *et al.*, *J. Pharmacol.*, 1940, 69, 166.

## SULPHONAL

*B.P.*



*Syn.* SULPHONMETHANUM (*P.G. VI, P. Helv. V, etc.*), DIETHYL-SULPHONEDIMETHYLMETHANE (*Fr. Cx.*).

[P1] "*Sulphonal; alkyl sulphonals.*"

[S1] "*Sulphonal; alkyl sulphonals.*"

[S4] "*Sulphonal; alkyl sulphonals.*"

*Dose.*—5 to 20 grains (0.3 to 1.2 g.), in cachets or suspended with mucilage. Should be finely powdered and followed by a draught of hot fluid. Unless in solution the dose should be given 1 to 2 hours or more before sleep is desired.

In colourless crystals or powder, tasteless and odourless. *M.p.* about 126°.

*Soluble* about 1 in 450 of water, 1 in 15 of boiling water, 1 in 80 of alcohol 90%, freely in hot alcohol, 1 in 90 of ether, 1 in 3 of chloroform.

*Antidotes.* Empty stomach by emetic or stomach tube. Keep patient lying down and warm, but keep him roused. Give sodium bicarbonate in dilute solution freely. Stimulants, *e.g.*, hot strong coffee, strychnine  $\frac{1}{4}$  gr., or caffeine sodium benzoate 2 gr., hypodermically. Nikethamide, 5 to 15 ml. of 25% solution, intravenously. Dextrose intravenously. Artificial respiration and inhalations of oxygen with 7% carbon dioxide if necessary. Lumbar puncture and drainage, to remove the poison which has passed into the cerebrospinal fluid, may be required.

*Uses.* Sulphonal is an hypnotic and is used for producing prolonged sleep in psychiatric cases and in nervous insomnia, especially when chloral is contraindicated. It is slow in taking effect, and is best given in hot milk three to four hours before retiring. The sleep produced lasts from six to eight hours and the effect of the drug may be carried over to the next day, with vertigo, lassitude, drowsiness and depression. Since it is very slowly absorbed and excreted it is cumulative, and must not be used continuously. It does not produce tolerance but it may cause a habit, symptoms of which are a general lethargy, mental, moral and muscular weakness, loss of nutrition, and dyspepsia. It may sometimes give rise to skin eruptions and to the appearance of hæmatoporphyrin in the urine. Sulphonal has only feeble analgesic properties and is of no value in insomnia due to pain.

[P1-81-84] **Methylsulphonal** (*B.P.*, *P. Ned. V*, *P.G. VI*, *F.E. VIII*). *Syn. and Prop. Name.* DIETHYLSULPHONEMETHYLETHYLMETHANE, SULFONETHYLMETHANUM (*U.S.P. XI*), METHYLSULFONALUM (*P. Belg. IV*, *P. Helv. V*), TRIONAL (*Bayer Products, London*).  $(\text{CH}_3)(\text{C}_2\text{H}_5)\text{C}(\text{SO}_2\cdot\text{C}_2\text{H}_5)_2 = 242\cdot3$ .

*Dose.*—5 to 20 grains (0·3 to 1·2 g.), in cachets, in a large cup of hot liquid. *P. Helv. V* max. single dose 15 grains, max. during 24 hours 30 grains. *U.S.P. XI* average dose 12 grains.

An oxidation product of mercaptol made by the condensation of methylethylketone with ethylmercaptan. In crystalline scales or microcrystalline powder, m.p. about 77°.

*Soluble* 1 in 320 of water, 1 in 12 of alcohol 90%, and in ether.

*Antidotes.* Treat as for poisoning by sulphonal, p. 973.

*Uses.* Has a stronger hypnotic action than that of sulphonal and produces sleep in half to one hour. Methylsulphonal is more effective in sleeplessness connected with neurasthenia and organic brain disease, but is useless in insomnia due to pain, and in morphine and cocaine habits. Toxic symptoms are the same as with sulphonal, but there is less likelihood of cumulative effect.

## SULPHUR

S = 32·06.

**Sulphur Præcipitatum** (*B.P.*, *U.S.P. XI*, *Fr. Cx.*). *Syn.* MILK OF SULPHUR.

*Dose.*—15 to 20 grains (1 to 4 g.), in milk or treacle, or as confection of sulphur with or without confection of senna. *U.S.P. XI* average dose 1 dr.

A soft powder free from grittiness, obtained by boiling sublimed sulphur with calcium hydroxide and water and decomposing the resulting solution with hydrochloric acid. Under a microscope it is seen to consist entirely of amorphous particles with no associated crystals. M.p. about 115°, forming a mobile liquid which darkens and becomes viscid on heating to 160°.

*Soluble* almost completely in carbon disulphide, also soluble in benzene, ether, chloroform, light petroleum and oil of turpentine.

*Uses.* Internally it has no action on the stomach but a certain proportion administered is converted into alkali sulphides in the intestines with consequent mild laxative effect. Given internally it has been employed for skin affections, occasionally benefiting chronic eczema with much itching. Externally, sulphur is commonly used to cure scabies and for acne. Sweating of the feet has been treated by drachm doses thrice daily.

**GONORRHOEA.** 132 cases treated with intramuscular injection of a suspension containing precipitated sulphur 1, guaiacol 5, camphor 10, eucalyptol 20, in oil of sesame to 100, the dose gradually increasing from 0·5 ml. to 4 ml. The injections are given at intervals of 4 to 6 days. A rise of temperature usually occurred in from 6 to 8 hours passing off in 12 to 24 hours. The course of the



disease was considerably shortened in most cases of epididymitis, but treatment was less successful in prostatitis.—G. Guldberg, per *Brit. med. J. Epit.*, ii/1936, 14.

**Balneum Sulphuris (B.P.C.).** Contains freshly precipitated sulphur obtained from 5 oz. each of sodium thiosulphate and sodium acid sulphate per 30 gallons.

**Confectio Sulphuris (B.P.).**

*Dose.*—1 to 2 drachms (4 to 8 g.).

Contains 45% of precipitated sulphur with 11% of potassium acid tartrate, tragacanth, syrup, glycerin and tincture of orange.

**Lotio Sulphuris (B.P.C.).**

Precipitated sulphur 30 gr. in glycerin, alcohol, rose water and solution of calcium hydroxide to 1 oz.

**Lotio Sulphuris (C.X.H.).**

Precipitated sulphur 20 gr., glycerin 10 m., industrial methylated spirit 15 m., lime water 2 dr., water to 1 oz.

**Lotio Sulphuris Composita (C.X.H.).**

Precipitated sulphur 15 gr., zinc sulphate 15 gr., sulphurated potash 15 gr., water to 1 oz.

**Lot. Sulphur. Co. (N.I.F.).** Precipitated sulphur 2 dr., glycerin 80 m., tincture of quillaia 30 m., industrial methylated spirit  $\frac{1}{2}$  oz., solution of calcium hydroxide to 8 oz.

**Trochisci Sulphuris (B.P.C.).**

*Dose.*—1 to 6.

Contain precipitated sulphur 5 gr. and potassium acid tartrate 1 gr. For skin and rheumatic affections.

Garrod's formula is 4 grains of precipitated sulphur with 1 gr. of potassium acid tartrate.

**Unguentum Sulfuris (U.S.P. XI).**

• Precipitated sulphur 15, wool fat 5, yellow wax 5, white petrolatum 75.

**Azudine (Lilly, London).** Precipitated sulphur 10%, phenol 1%, with camphor, menthol and balsam of Peru in an ointment base.

**Sulphur Sublimatum (B.P., U.S.P. XI, Fr. Cx.).** *Syn.* FLOWERS OF SULPHUR.

A slightly gritty powder. Under a microscope is seen to consist chiefly of rounded amorphous particles or aggregates occasionally associated with semi-crystalline masses.

**Soluble** almost completely in carbon disulphide, about 1 in 4 of petrol, benzene or toluene, about 1 in 70 of chloroform, 1 in 125 of almond oil, 1 in 200 of olive oil or cotton-seed oil, 1 in 70 of sesame oil. Insoluble in water or alcohol 90%.

**Uses.** Is used for the same purposes as precipitated sulphur, especially in ointments for skin affections and for scabies. Dusted between the toes it destroys the fungus producing epidermophytosis. A full dose of sulphur administered at night to patients before and while undergoing mercurial treatment for syphilis prevents mercurial stomatitis. A 1 or 2% solution of sulphur in olive oil administered by intramuscular injection is used for the production of artificial pyrexia in the treatment of general paralysis of the insane, various forms of arthritis and in dementia præcox. The initial dose is 0.5 ml., and injections are given on alternate days, increasing by 0.5 ml. up to a maximum of 5 ml. The aim is to reach a temperature of 104°F. gradually. A 1% aqueous suspension is also sometimes used.

**CHRONIC NON-SPECIFIC ARTHRITIS.** Treatment of 50 cases by intramuscular injection of Sulfosin, starting with 0.5 ml., after which further injections are given every 5 or 8 days in steadily increasing amounts up to (usually) 4 or 5 ml. After the third dose, massage, passive movement, and some form of heat therapy found useful between injections. Results show that considerable improvement may be expected in a proportion of patients in whom the changes are limited to the soft structures about the joint and are not permanent in nature, but less improvement when damage of a permanent kind is present. Treatment should not be given during the acute phase in elderly, feeble, emaciated, nervous or very obese patients, or in patients with active organic disease other than arthritis.—D. Krestin, *Brit. med. J.*, ii/1935, 1144.

**Colsul** (*Crookes Laboratories, London*). 1% solution of sulphur in vegetable oil; also a 1% aqueous colloidal suspension. *Dose*.— $\frac{1}{4}$  ml. initially increased at each injection by  $\frac{1}{4}$  ml. to a maximum of 5 ml. or until a sufficient degree of pyrexia is obtained (10 to 12 ml. have been used).

**Sulfosin** (*Leo, Copenhagen; Bencard, London*). Solution of sulphur in oil for artificial fever therapy.

[P1] **Neo-Sulfosin** (*Leo, Copenhagen; Bencard, London*). Sublimed sulphur 0.5, guaiacol 0.5, camphor 1, Anæsthesin 4, almond oil to 100. Used for the same purpose as Sulfosin.

**Sulphur Lotum** (*U.S.P. XI, P. Helv. V*) is sublimed sulphur washed with ammoniated water.

**Sulphur Nigrum** was the name formerly applied to native Sicilian sulphur. It is now applied to the residuum from the subliming pots, or to sublimed sulphur mixed with charcoal. Is used in veterinary medicine.

**Unguentum Picis et Sulphuris** (*L.H.*). *Syn.* WILKINSON'S OINTMENT.

Sublimed sulphur 2 dr., tar 2 dr., potash soap 4 dr., benzoinated lard 4 dr., purified talc 1 dr.

**Unguentum Sulphuris** (*B.P.*).

Sublimed sulphur 10% in yellow simple ointment.

Scabies is treated by sulphur ointment after washing with soft soap. Use equal parts of the *B.P.* ointment and soft paraffin.

**Unguentum Sulphuris Camphoratum** (*B.P.C.*).

Sulphur 2% with phenol, resorcinol, camphor and solution of coal tar in lard and white soft paraffin.

**Unguentum Sulphuris Compositum** (*B.P.C.*).

Sublimed sulphur 15%, tar 15% and calcium carbonate 10%, in lard and soft soap.

[P1] **Unguentum Sulphuris cum Hydrargyro** (*U.C.H.*).

Sublimed sulphur 30, sublimed mercuric sulphide 2, ammoniated mercury 2, arachis oil 12, lard 54. Useful in skin diseases.

**Unguentum Sulphuris et Resorcinolis** (*B.P.C.*). Sulphur 4.5% and resorcinol 3% in yellow soft paraffin.

**Unguentum Sulphuris et Zinci cum Kaolino.** Sulphur 4, zinc oxide 3, kaolin 1, benzoinated lard 8. For sweating of the feet.

**Sulphuris Chloridum** (*B.P.C.*). *Syn.* SULPHUR MONOCHLORIDE.  $S_2Cl_2 = 135.0$ .

A reddish-yellow mobile fuming liquid with disagreeable penetrating odour. Decomposed by water or moist air, giving sulphur and hydrochloric and sulphurous acids.

**Unguentum Sulphuris Hypochloritis** (*B.P.C.*).

Sublimed sulphur 12% and sulphur chloride 2%, with oil of bitter almonds (*s.A.P.*), in lard. For scabies.

**ACNE ROSACEA.** Sulphur hypochlorite ointment (*B.P.C.*) is a very useful ointment in this condition, but it is a very strong application and may aggravate

the irritation, especially in the dry cases. The patients usually feel uncomfortable for the first 24 hours, but after that the ointment produces astonishingly quick and marked improvement. If it is still annoying the skin after three days it should be discontinued.—S. Thomson, *Med. Pr.*, ii/1939, 471.

**Sulphuris Iodidum** (B.P.C.). *Syn.* SULPHUR SUBIODIDE.

A greyish-black crystalline solid containing not less than 70% of I.

**Unguentum Sulphuris Iodidi** (B.P.C.). Sulphur iodide 4% in glycerin and simple ointment. Used in acne rosacea, tinea and other parasitic skin diseases.

**Contramine** (*British Drug Houses, London*). Diethyl-ammonium-di-ethyl-dithio-carbamate,  $\text{SNH}_2(\text{C}_2\text{H}_5)_2\text{CSN}(\text{C}_2\text{H}_5)_2$ ,  $\text{M} = 222.3$ .

Occurs as white crystals, soluble 1 in  $2\frac{1}{2}$  of water, and available in ampoules of sterile solution for intramuscular injection. It is used in the chronic complications of gonorrhoea, including stricture, chronic epididymitis, conjunctivitis and iritis, and varied forms of chronic rheumatism.

*Dose.*—Intramuscularly  $\frac{3}{4}$  grain (0.05 g.) to 4 grains (0.25 g.) in 1 to 2 ml. of cold sterilised water or saline. Must not be heated.

The usual initial dose (intramuscularly) is 0.125 g. in 1 ml.

**Contramine Pessaries** are prepared for use in chronic cervicitis and endometritis. Bougies and suppositories are also made.

Local application of Contramine solution may assist healing of chronic ulcers. In cases of sinuses in muscles, closure is often obtained by intramuscular injections around the lesion.

In severe cases of metal intoxication 0.125 g. may be injected intramuscularly every day till 6 or more doses have been given. In other cases 2 injections of 0.125 g. with a week's interval usually suffice.

**Mesulphen.** *Syn. and Prop. Names.* DIMETHYLTHIANTHRENE, MITIGAL (*Bayer Products, London*), SUDERMO (*Burroughs Wellcome, London*).

Dimethyl-diphenylene-disulphide, a liquid compound containing 25% of sulphur. It is a yellow, odourless, neutral oil, soluble in chloroform and acetone. For the treatment of skin diseases by local application.

### Colloidal Sulphur.

Colloidal sulphur solution may be prepared by the decomposition of a mixture of sodium sulphide and sodium sulphite with acid in the presence of protective colloid.

For use in rheumatic and skin affections and wherever sulphur is indicated through excessive elimination.

**RHEUMATOID ARTHRITIS.** From a study of the clinical data it is concluded that the administration of colloidal sulphur, whether in small or large doses, does not alter the course of rheumatoid arthritis. Evidence is cited which proves that a primary disturbance of sulphur metabolism does not exist in patients with rheumatoid arthritis.—N. R. Abrams and W. Bauer, *New Engl. J. Med.*, i/1940, 541.

**Colloidal Sulphur B.R.I.** (*British Drug Houses, London*). A colloidal sulphur complex for administration by intramuscular or intravenous injection in the treatment of arthritis.

**Sarceptol** (*Anglo-French Drug Co., London*). Colloidal sulphur compound for local application in seborrhoea, scabies, eczema, alopecia, etc.

### Sulphuretted Hydrogen Poisoning.

Encountered in industries such as artificial silk works, chemical works, sewage works, etc.; it is stated that the maximum safe concentration for 6 hours may be taken as 1 in 20,000, but to avoid eye irritation and general lowering of health, it is advisable to keep it well below this.

**Antidotes.** Place patient in fresh air, apply artificial respiration and keep it up steadily. Inhalations of oxygen with 7% carbon dioxide. Give stimulants carefully; coffee by rectum if patient

cannot swallow. Iodised starch (5% iodine rubbed into starch with a little water and dried) has been suggested. Inhalation of chlorine recommended.

#### **Colloidal Selenium.**

Colloidal solutions of selenium have been advocated in the treatment of inoperable cancer.

For a full description of the selenide treatment of cancer, see A. T. Todd, *Brit. J. Surg.*, 1934, 619. See also A. T. Todd, *Med. Pr.*, Oct. 21, 1936 (supplement). See also *Lead Selenium Colloid*, p. 858.

**Radio-Active Selenide** (*British Drug Houses, London*). *Syn. R.A.S.* A feebly radio-active preparation, made by combining certain radium residues with selenium, for use in the treatment of cancer by the Bristol Royal Infirmary methods.

**Collôid Sulphur-Selenium, B.R.I.** (*British Drug Houses, London*). *Syn. SSE.* A double colloid of sulphur and selenium for use in conjunction with R.A.S.

The report of an investigation by the Medical Committee of the Royal Cancer Hospital on the treatment of 70 cases of cancer between October, 1934, and August, 1935, with colloidal selenium. Of the 70 cases treated, 41 have died, 21 are still under treatment, 7 have refused further treatment, and 1 who received merely prophylactic treatment is still without evidence of recurrence. Of the 41 cases which died, in 37 the treatment appeared to have no effect whatever, and in 4 there was transient alleviation of pain. Of the 21 cases still alive, in 3 the growth appears stationary, in 2 there was temporary diminution not maintained, in 10 there was definite alleviation of pain and improvement of the general condition, and in 6 the period of observation was too short for results to be shown.—*Lancet*, i/1936, 1198.

The dosages of colloid were far too low, and chemical alteration occurred during injection; the X-ray dosage was standardised, and, with the low dosage of colloid, must have been almost inoperative. A comparison of the method described with the original should have shown such discrepancies that to call it an independent test is far from the truth.—A. T. Todd, *Lancet*, i/1936, 1262.

**Colloidal Tellurium, B.R.I.** (*British Drug Houses, London*). A colloidal preparation of tellurium for administration by injection in the treatment of chronic rheumatism.

## **SUPPOSITORIA**

Suppositories are medicated masses intended for anal administration. They are usually conical at one end, the other end being flat so that the suppository is retained more easily by the sphincter muscle after insertion. It is customary to employ moulds which hold 1 g. (15 gr.) or 2 g. (30 gr.) of oil of theobroma. Unless otherwise specified, the 15-gr. size is supplied.

The bases employed for suppositories are oil of theobroma, glycerin suppository mass and occasionally freshly prepared soap, as in glycerin soap suppositories. It is essential that the melting-point of any suppository mass shall be between 30° and 35°. Oil of theobroma is usually employed unless the prescriber otherwise directs, and when the suppositories are prepared by melting and moulding, care should be taken not to overheat this base since, as with many other substances, overheating will cause a lowering of the solidifying-point and subsequent difficulty in setting. Because of this it is preferable to use powdered or shredded oil of theobroma. Certain medicaments such as phenol, chloral hydrate and resorcinol cause an appreciable lowering of the melting-point of oil of theobroma when warmed with it. In

preparing such suppositories, the melting-point may be brought back to normal by incorporating a little white wax. This addition may be avoided, except in the case of suppositories containing volatile oils, by using the minimum amount of heat.

Glycerin suppository mass has a limited use as a base because its gelatin content renders it incompatible with certain medicaments, particularly tannins. Ichthammol will occasionally form a water-insoluble mass which does not melt below body temperature. A 1 g. (15 gr.) mould will hold 1.2 g. (18 gr.) of glycerin suppository mass. If the large proportion of glycerin present in the mass is not desired, the following basis is a good substitute: Gelatin 10 g., water 40 ml.; soak, dissolve with gentle heat, add glycerin 15 g., and evaporate on a water-bath until the mass weighs 25 g.

### ***Suppository Mass for Hot Climates.***

Oil of theobroma is generally used, and it is customary to incorporate varying quantities of white wax according to the prevailing temperatures. 5 to 15% is commonly employed. Different samples of both oil of theobroma and white wax may each have different melting-points, so that variation will occur in mixtures. Using an oil of theobroma with m.p. 33-89° and white wax with m.p. 61°, the melting-points of mixtures are as follows:—

White Wax.			Melting Point.	
2½	..	..	..	32.6°
4.5	..	..	..	33.06°
10	..	..	..	39.44°
15	..	..	..	46.11°
20	..	..	..	50.00°

Suppositories should be sent out in partitioned boxes lined with waxed paper, and, when made with glycerin suppository mass, they should be slightly greased with oil. When they contain volatile and hygroscopic ingredients, or when intended for export to tropical climates, they should be wrapped separately in tinfoil.

In tropical countries the use of hardening agents such as beeswax is not recommended, since the transition temperature becomes too close to the temperature at which the mixture softens sufficiently to mould suppositories. In temperate climates hardening agents may be satisfactory, but for the extemporaneous dispensing of suppositories in the tropics they are useless. Hydrogenated palm kernel oil, m.p. 40° to 42°, is suitable for use as a base, and in cases where it is too soft owing to a high temperature, or where the melting-point is lowered by soluble medicaments, it may be hardened by the addition of hydrogenated soya bean oil, m.p. 56°, or beeswax. For general use in Malaya in suppositories containing no soluble medicament the addition of 5% of hardened soya bean oil is satisfactory, but if fat soluble substances are present the amount of hardening agent must be increased. It is recommended that the formulæ in the *B.P.* and *B.P.C.* should be modified, since they are of no assistance in the present form to dispensers in warm countries.—A. F. Caldwell, *Quart. J. Pharm.*, 1939, 680.

**Buginaria.** Bougies are medicated pencils intended for insertion into the urethra, nostrils or ears. They are prepared in the same way as suppositories but differ in shape, resembling a pointed rod.

**Urethral Bougies** are usually in two sizes: (a) 2 inches and weighing 15 gr., or (b) 4 inches and weighing 40 gr. If the size is not specified by the prescriber, it is usual to supply the smaller size. Metal moulds can be obtained to give these sizes.

The basis may be either gelato-glycerin or oil of theobroma. A suitable gelato-glycerin base may be prepared from the following formula:—Gelatin 32.5 g., glycerin and water of each 40 ml. Incorporate and evaporate to 100 g. Bougies made with this basis are directed to be dipped in warm water prior to insertion. When prepared with theobroma basis, bougies may be made by other methods than moulding. Thus the medicament may be incorporated in the basis by massing in a pill mortar, afterwards piping the mass on a pill machine and shaping one end with the fingers. If this method is adopted it may be advisable to incorporate about 5 to 10% of wool fat. Lubricated glass tubing of suitable diameter may be used as a bougie mould, the melted mass being sucked up into it, allowed to solidify, then pushed out with a glass rod and cut to the correct length, one end being subsequently pointed. Urethral bougies are sometimes known as *cereoli*.

**Nasal Bougies** are usually made with a gelato-glycerin basis. They are 1 inch long and weigh about 10 grains.

**Aural Bougies** are made with an oil of theobroma basis unless otherwise ordered. They are usually conical in shape, and weigh about 5 gr. Bougies for the ear are sometimes known as *aurinaria*.

**Pessi.** Pessaries are medicated masses intended for insertion into the vagina. They may be made with a basis of oil of theobroma or glycerin suppository mass. If the basis is not specified, it is usual to use oil of theobroma. Pessaries produce a continued action on the parts in leucorrhœa, also for ulceration and inflammation of the cervix uteri. They are usually prepared like suppositories by moulding, the mould having an oil of theobroma capacity of 8 g. (120 gr.). The shape may be convex or suppository-shaped.

To be efficient, pessaries must be inserted as far as possible whilst the patient is in the supine position with the hips raised. They are most effectual at bedtime.

**Ovula** (*Fr. Cx.*) are ovoid pessaries prepared with a glycerin-gelatin or oil of theobroma basis.

#### ***Pessary Mass for Hot Climates.***

Mixtures of white wax and oil of theobroma are usually used (*see* suppositories, p. 979).

**Tampons.** Consist of plugs of non-absorbent cotton-wool, globular in shape, about  $1\frac{1}{2}$  in. in diameter, and covered with gauze. They are medicated by saturating them in a solution of the medicament, the usual solvent being glycerin.

**Glycerin Tampons.** Saturated with glycerin. **Mild Silver Proteinate Tampons,** containing 1, 5 and 10% mild silver

proteinate in glycerin. **Ichthammol Tampons** saturated with 5, 10 or 20% ichthammol in glycerin. **Iodoform Tampons**, with 5% iodoform in glycerin.

**Pontampons** (*Pontampon Co., London*) consist of a semi-solid slowly-soluble medicated cone with a non-absorbent wool tampon attached, the whole encased in a soluble gelatin shell.

For the treatment of gonorrhœa, endometritis, cervicitis, vaginitis, leucorrhœa, dysmenorrhœa, prolapsus uteri. Numerous medicated products are available.

## TABELLÆ

### COMPRESSED TABLETS

Tablets of medicaments are usually preferable to pills, since less excipient is required and the risk of not disintegrating in the alimentary tract is lessened. They may be of several types.

(a) **Easily friable and readily disintegrated after swallowing**, for such substances as acetylsalicylic acid, phenazone, phenacetin. This type is obtained by using the minimum amount of compression and incorporating from 5 to 15% of potato starch.

(b) **Hard Tablets** which slowly disintegrate or dissolve. These are obtained by using heavy compression which produces a tablet resembling a lozenge. Substances such as potassium chlorate or bromide, and ammonium chloride are made into tablets of this type. They are intended either to be dissolved slowly in the mouth or to be dissolved in water and taken as a draught.

(c) **Solvellæ**, or solution-tablets, which are intended to be dissolved in water for external or local use. When they contain poisonous ingredients a suitable dye is often added to distinguish them.

(d) **Tablet-triturates**. These are small tablets made with the minimum of compression in special metal or vulcanite moulds and intended to be crushed to powder before use. They consist of substances such as mercury with chalk, calomel, etc., which are usually prescribed as powders.

(e) **Hypodermic Tablets**. These are very small tablets, machine-made, readily soluble in water, and used for the preparation of subcutaneous injections. They contain a basis of sterilised lactose, and are made and packed under controlled aseptic conditions.

**Preparation of Tablets.** Fine powders will not compress to tablets, and it is necessary to convert such material into granules. If, however, the medicament is in the form of small crystals no further preparation is necessary. Thus, such substances as potassium bromide, chlorate or permanganate, sodium chloride, heavy crystal forms of acetylsalicylic acid, phenacetin, and phenazone only require drying and passing through a No. 16 sieve and any loose powder shaking out on a No. 30 sieve. The material can then be fed directly into the machine or, if a friable tablet be required, mixed with 5 to 15% of potato starch, and then compressed.

In the preparation of granules, it is necessary to add some liquid which will damp the mass so that it will cohere in small lumps on passing through a No. 16 sieve and remain as hard granules on drying. The liquid used will vary with

the medicament. A little alcohol is suitable for material which contains alcohol-soluble constituents, for example alcoholic extracts such as the dry extracts of belladonna and hyoscyamus.

By the use of vacuum drying it is possible to produce a dry mass in a very porous condition, so that on passing through a No. 16 sieve, granules quite suitable for immediate use in the tablet machine are obtained. Dry extract of cascara may be made suitable for tablet granules in this manner. The method could probably be extended to other similar extractives.

A general excipient which will be efficient in the majority of cases is a mixture of equal parts of syrup and dilute (1 in 4) mucilage of acacia. This is thoroughly worked into the powdered medicament until sufficient is present to give coherence on passing. It is then passed through a No. 16 sieve and dried at a temperature of about 40° in a drying oven. The mass is then resieved through the No. 16 sieve and loose powder shaken out on a No. 30 sieve. It is often advisable to include a little starch in the powder before granulation in order to ensure disintegration on swallowing.

In order to prevent sticking in the machine and to give an easy flow, from 1 to 3% of finely powdered French chalk may be added to the dry granules, as a lubricant, by shaking. Other lubricants may be used. Thus for tablets intended for the preparation of aqueous solutions, boric acid may be substituted. Liquid paraffin sprayed on to the granules is also used, and an emulsion of oil of theobroma has been recommended, but the oil of theobroma goes rancid on storage.

It is important that granules shall be of even size, free from much loose powder and *thoroughly dry*. Much of the trouble in tablet making results from neglecting the latter precaution.

In using the tablet machine, whether hand or power-driven, it is advisable to keep the punches in good condition. They should be kept well polished, if possible by "buffing" them on a polishing machine. An ordinary cork spiked on to the axis of the polishing machine and used with a trace of very fine emery powder forms a very suitable "buffing" surface. This precaution will tend to prevent "capping" or the splitting off of the surface of the tablet.

Owing to the necessity of granulating, tablets are rarely the same weight as the medicament. Thus a 5-grain tablet usually weighs from 5½ to 6½ gr.

Tablets introduced into the B.P. should be standardised with regard to the amount of medicament contained, the size and final weight, and the rate of disintegration. The latter is important, particularly when tablets of potent substances are to be swallowed whole. Many types of disintegration tests have been suggested, but most of them fail in not having a definite end-point. The new method described in this paper, which depends upon a weighted wire cutting through the tablet after the latter has been softened in water, overcomes this disadvantage, the end-point being the fall of the weight. Probably the chief factors affecting the rate of disintegration of tablets are the formula used in the preparation of the granules, particularly the type of binding agent, disintegrator and lubricant, and the age of the tablets, whilst speed and degree of compression, size, shape and weight of tablet, etc., also have a considerable influence. The rate of disintegration has been investigated for a considerable range of tablets and reasons are suggested for the variations observed.—H. Berry, *Quart. J. Pharm.*, 1939, 501. See also C. L. M. Brown, *ibid.*, 589, for a further method of testing.

**Tablet-triturates.** The mould consists of two plates, one with perforations and another with pegs corresponding in size and position with the perforations. If the medicament has a small dose, such as calomel or strychnine hydrochloride, it is necessary to make a dilution with lactose to give bulk. The powder is then dampened with 60% alcohol to give coherence and passed into the perforations. A spatula is used to ensure complete filling of each cavity and to smooth off excess. The filled plate is superposed on the pegs and pressed down, leaving damp tablets on the latter. The tablets are then dried. In order to ascertain the capacity of the mould, a few trial tablets must be made. Moulds are made in a range of sizes ½ to 4 grains, and will prepare 50 to 250 tablets at one time.

Notes on the manufacture of tablets.—*Pharm. J.*, ii/1935, 475, 503.

Details of the preparation of some types of tablet-triturates commonly in demand are described, together with the variations observed in the properties of such triturates when the proportion and strength of alcohol, the temperature of drying and quantity and nature of the active medicament vary.—G. W. G. Smithers, *Quart. J. Pharm.*, 1939, 478.



**Trochisci.** Lozenges consist of sugar bases containing gum, which causes the mass to set hard on drying. The medicaments in lozenges are usually those having a local action on the throat, but in some cases, such as sulphur and bismuth lozenges, they afford a convenient method of giving the drugs. The following are the usual bases employed and the lozenges made from them.

**GENERAL BASIS.** This is the official basis for lozenges in the *British Pharmacopœia*, and consists of sucrose and acacia flavoured with tincture of tolu. Tannic acid, extract of krameria, krameria and cocaine, morphine, morphine and ipecacuanha.

**FRUIT BASIS.** A basis flavoured with black currant. Benzoic acid, compound ammonium chloride, catechu, guaiacum resin, eucalyptus.

**ROSE BASIS.** A basis flavoured with oil of rose. Potassium chlorate, compound bismuth.

**SIMPLE BASIS.** An unflavoured basis. Antacid, reduced iron, liquorice (Brompton cough lozenge), ipecacuanha, santonin.

(For composition and uses of various B.P., B.P.C., and other lozenges, see under the drug.)

## THEOBROMATIS SEMEN

(with THEOBROMINE and THEOPHYLLINE)

B.P.C.

Syn. CACAO OR COCOA SEED.

The seeds of *Theobroma Cacao* (Sterculiaceæ) containing in the kernel about 1 to 3% of theobromine, a small amount of caffeine and 40 to 60% of fat. The shell contains about  $\frac{1}{2}$  to 2% of theobromine. When heated and deprived of husk and membrane, these yield cocoa nibs. The nibs with most of the oil pressed out produce, when reduced to powder, cocoa for use as a beverage. Before expression of fat the seeds may be treated with an alkali, and flavouring such as vanillin may also be added.

**Oleum Theobromatis** (B.P., U.S.P. XI, P. Helv. V). Syn. CACAO BUTTER, COCOA BUTTER, CACAO OLEUM (P. Belg. IV).

The concrete oil of the seeds (yield about 45%). M.p. about 30° to 35°, i.e., below the temperature of the body. It is therefore much used for suppositories. For substances which lower the melting-point of the oil, and for export to hot climates, it is well to add 5 to 15% of white wax. (See Suppositories.)

**Soluble** freely in ether, chloroform, benzene, carbon disulphide and light petroleum; slightly soluble in alcohol 90%.

To deodorise for cooking, heating the oil in an open pan to 188° for 5 minutes has been suggested, and, to give it the consistence of butter, adding 5 parts of cotton-seed oil to each 4 parts of cacao butter has been recommended.

**Pasta Theobromatis.** Syn. CHOCOLATE.

This is made by grinding the nibs into a paste, with sugar and vanilla or other flavouring added; it contains about 40 to 60% of sugar and about 28 to 38% of fat.

**Postonal**, a wax-like polymerisation product of ethylene oxide, is used as a substitute for cocoa butter in Germany. It melts at 60°, is soluble in 10 parts of water, and resorption of Postonal suppositories is stated to be better than the resorption of those made with cocoa butter.—per *Pharm. J.*, i/1940, 172.

**Theobromina** (*B.P.C.*, *P. Helv. V*, *Fr. Cx.*, *P. Ned. V*).  
*Syn.* 3 : 7-DIMETHYLXANTHINE, SANTHEOSE.

$C_7H_8(CH_3)_2O_2N_4 = 180.1$ .

*Dose.*—5 to 10 grains (0.3 to 0.6 g.).

A white, crystalline, neutral powder with bitter taste.

**Soluble** 1 in 1000 of water, 1 in 115 of boiling water, 1 in 1400 of alcohol 90%; sparingly soluble in chloroform and ether; insoluble in benzene. 2% aqueous solutions may be obtained with aid of trisodium phosphate.

**Uses.** Theobromine is similar in action to caffeine, but has less effect on the central nervous system and a more pronounced effect on the heart and kidneys. It is used principally as a diuretic, especially for the removal of cardiac effusions, in which connection it is often prescribed in association with digitalis. It may also be used in renal or hepatic effusions, though its efficiency in these is less certain and it is contraindicated in acute nephritis, since it may cause renal irritation. It may be employed in angina pectoris; doses of 20 to 30 gr. spread over twenty-four hours are stated to lessen the frequency and severity of attacks.

**Theobromine Calcium Salicylate.** *Syn. and Prop. Names.*  
THEOCALCINE, CALCIUM-DIURETIN (*Knoll, London*; *Savory & Moore, London*), CALCOTHEOBROMINE (*Richter, London*).

*Dose.*—7 to 15 grains (0.5 to 1 g.).

A white powder slightly soluble in water, containing about 48% of theobromine and 11% of calcium. Prepared similarly to the sodium salt from theobromine, calcium oxide and calcium salicylate.

**Uses.** Similar to theobromine. For arteriosclerosis 30 grains have been given daily, and up to 75 grains daily to achieve diuretic effect. It is also stated to be a preventive of asthmatic attacks.

**Raminal** (*Napp, London*). Tablets containing theobromine calcium salicylate  $1\frac{1}{2}$  gr., chlorophyll  $\frac{1}{2}$  gr., iron phosphate  $\frac{1}{2}$  gr. *Dose.*—2 tablets thrice daily. Hypertension, angina pectoris, arteriosclerosis, cardiac asthma.

[P1-81] **Vasobroman** (*Richter, London*). Tablets containing theobromine calcium salicylate 0.25 g., papaverine hydrochloride 0.01 g., bromoisovaleryl-carbamide 0.2 g. *Dose.*—1 tablet thrice daily. Arteriosclerosis and hyperpiesis.

**Iod-Calcium-Diuretin** (*Knoll, London*; *Savory & Moore, London*). Tablets containing  $7\frac{1}{2}$  gr. of Calcium-Diuretin and  $1\frac{1}{2}$  gr. of potassium iodide. *Dose.*—1 thrice daily after food; may be increased temporarily to 2 tablets thrice daily. As improvement sets in, the smaller dose should be resorted to and may be maintained for lengthy periods. In hypertonia, angina pectoris and asthma.

**Iodcalcotheobromine** (*Richter, London*). Theobromine calcium salicylate 0.25 g., potassium iodide 0.05 g. *Dose.*—3 tablets daily. Arteriosclerosis, hypertension, etc.

**Rhodan-Calcium-Diuretin** (*Knoll, London*; *Savory & Moore, London*). Tablets containing  $7\frac{1}{2}$  gr. of Calcium-Diuretin and  $1\frac{1}{2}$  gr. of potassium thiocyanate. *Dose.*—1 tablet thrice daily after food; 2nd and 3rd weeks, 1 tablet twice daily; 4th, 5th and 6th weeks, 1 tablet once daily. Crush in a little water or milk before swallowing. For treatment of hypertonia of climacteric or sclerotic origin, and in renal cases.

**Theobromina et Sodii Acetas.** *Prop. Name.* AGURIN (*Bayer Products, London*).

*Dose.*—10 to 15 grains (0.6 to 1 g.), up to 45 grains daily in fresh solution.

White, crystalline, hygroscopic powder consisting of a mixture of sodium acetate with the sodium derivative of theobromine.

**Soluble** 1 in 2 of water and about 1 in 200 of alcohol 90%.

Its action resembles that of theobromine, but it has the advantage of greater solubility and of being well tolerated by the stomach. Not to be given with acid substances, nor with sugar or gum, and in general incompatible as for theobromine and sodium salicylate. To be preserved from the air, the  $\text{CO}_2$  of which tends to decompose it.

**Theobromina et Sodii Salicylas** (*B.P., U.S.P. XI, P. Helv. V, etc.*) *Prop. Name.* DIURETIN (*Knoll, London; Savory & Moore, London*).

*Dose.*—10 to 20 grains (0.6 to 1.2 g.). *P. Helv. V* has max. in 24 hours 90 grains approx.

A mixture of sodium theobromine ( $\text{C}_7\text{H}_7\text{NaO}_3\text{N}_4$ ) and sodium salicylate ( $\text{C}_7\text{H}_5\text{O}_3\text{Na}$ ) in approximately molecular proportions. It is rapidly decomposed in moist air with absorption of  $\text{CO}_2$  and liberation of theobromine—hence less soluble in water. It must be kept in stoppered bottles.

**Soluble** 1 in 1 of water; insoluble in alcohol 90%, chloroform and ether.

**Incompatible** with ammonium salts, sodium bicarbonate and all acid salts, alkaloidal salts, free inorganic and organic acids, and aromatic spirit of ammonia.

**Uses.** Its actions resemble those of theobromine. It is especially valuable as a diuretic in cardiac dropsy and chronic Bright's disease. Has prolonged effect when given with digitalis. In angina pectoris it lessens the frequency of attacks.

**ANGINA PECTORIS.** Purine-base diuretics are of value, but little to choose between any of the theobromine preparations. To avoid tolerance over a long period, the following (or some of them) were used on alternate weeks:—Theobromine 5 gr., theobromine sodium acetate 10 gr., theobromine sodium salicylate 10 gr., theobromine calcium salicylate  $7\frac{1}{2}$  to 10 gr., theophylline 2 gr., theophylline sodium acetate 4 gr., theophylline-ethylenediamine  $1\frac{1}{2}$  to 3 gr. Four doses daily usually given (often best taken in the middle of a meal) for the first 4 days of each week. Will not give complete relief, but more helpful than any other drugs used.—N. C. Gilbert and J. A. Kerr, *J. Amer. med. Ass.*, i/1929, 202.

In a comparative evaluation of various theophylline and theobromine preparations in the treatment of angina pectoris, the sodium acetate derivatives were found to be the most effective preparations. Patients who did not respond to these drugs usually showed a good response to theophylline with calcium salicylate, which was the next best preparation.—M. G. Brown and J. E. F. Riseman, *J. Amer. med. Ass.*, ii/1937, 256.

**Tabellæ Theobrominæ et Sodii Salicylatis** (*B.P.C.*) contain  $7\frac{1}{2}$  gr. (0.5 g.).

**Theophyllina** (*B.P. Add. I, U.S.P. XI, P. Helv. V, Fr. Cx.*). *Syn.* 1:3-DIMETHYLXANTHINE.  $\text{C}_8\text{H}_{10}(\text{CH}_3)_2\text{O}_2\text{N}_4 \cdot \text{H}_2\text{O} = 198.1$ .

*Dose.*—1 to  $2\frac{1}{2}$  grains (0.06 to 0.15 g.). No dose is given in *B.P. Add. I*.

White crystalline powder obtained from tea, or prepared synthetically. M.p.  $269^{\circ}$  to  $272^{\circ}$ .

**Soluble** 1 in 160 of water, 1 in 120 of water at  $25^{\circ}$ , 1 in 100 of alcohol 90%, 1 in 80 of alcohol 95% at  $25^{\circ}$ , 1 in 86 of chloroform. Readily soluble in alkali hydroxide solutions. Sparingly soluble in ether.

More strongly diuretic than theobromine, and also more irritant to the stomach. It has been employed intravenously in the treatment of adrenaline-resistant cases of asthma, and is claimed to give prompt and prolonged relief.

The most effective of the xanthine diuretics. Best given in two doses of 0.3 to 0.5 g. with half a glass of water at 7 and 10 a.m.—H. A. Christian, *New Engl. J. Med.*, i/1936, 419.

**CORONARY ARTERY DISEASE.** In the treatment of congestive failure due to disease of the coronary arteries the preparations of theophylline are amongst the most effective remedies. The action is prompt and generally evident in those cases in which it is possible to restore cardiac function, provided the work of the heart is reduced to a minimum. It is given in doses of  $1\frac{1}{2}$  to 3 grains after meals and continued after the patient leaves hospital. Not all cases of coronary artery disease are benefited, but in some the improvement is dramatic.—F. M. Smith, H. W. Rathe and W. D. Paul, *Arch. intern. Med.*, 1935, 56, 1260.

**Theamin** (*Lilly, London*). Theophylline monoethanolamine. Capsules contain 3 grains. Also issued in ampoules for intravenous use (0.25 g. in 10 ml.) or for intramuscular use (0.5 g. in 2 ml.).

**Theophyllina et Sodii Acetas** (*B.P., U.S.P. XI, P. Helv. V*). *Prop. Name.* THEOCIN SODIUM ACETATE (*Bayer Products, London*).

**Dose.**—2 to 5 grains (0.12 to 0.3 g.) dissolved in water, 3 or 4 times daily after meals. Nausea may be prevented by small doses of menthol beforehand, e.g.,  $\frac{1}{10}$  gr. in 15 m. of tincture of orange.

A white, crystalline powder obtained by mixing solutions of equimolecular proportions of sodium theophylline and sodium acetate and evaporating to dryness.

**Soluble** 1 in about 25 of water; insoluble in alcohol 90%, ether or chloroform.

**Incompatible** with acids, ammonium salts and sodium bicarbonate.

**Uses.** A soluble compound for the administration of theophylline. It is a more potent diuretic than theobromine, but is more liable to cause gastric disturbance.

**Theophyllina cum Æthylenediamina** (*U.S.P. XI*). *Syn. and Prop. Name.* AMINOPHYLLINE, METAPHYLLIN, CARDOPHYLLIN (*Whiffen, London*) (formerly marketed under the German proprietary name EUPHYLLIN).

**Dose.**—Orally,  $1\frac{1}{2}$  to 3 grains (0.1 to 0.2 g.) thrice daily; rectally,  $5\frac{1}{2}$  grains (0.36 g.) as a suppository or retention enema; intramuscularly,  $7\frac{1}{2}$  grains (0.48 g.) in 2 ml.  $3\frac{3}{4}$  grains (0.24 g.) may be given intravenously in emergency in 10 ml. of sterile water. *U.S.P. XI* average dose  $1\frac{1}{2}$  grains.

White or slightly yellowish granules with a slight ammoniacal odour and bitter taste, prepared by dissolving theophylline in ethylenediamine and evaporating to dryness. To be stored in air-tight containers.

**Soluble** 1 in 5 of water (at 25°); insoluble in alcohol and ether. Aqueous solutions absorb carbon dioxide readily from the air with the liberation of theophylline.

**Uses.** Has the properties of theophylline with the advantage of greater solubility and consequently greater rapidity of action. In addition to its use as a diuretic in cardiac and renal oedema and eclampsia, the compound is also of value in cardiac asthma, angina pectoris and Cheyne-Stokes breathing, and when given intravenously relieves the dyspnoea of cardiac failure. It promotes coagulation of the blood and has been found useful in hæmoptysis and other hæmorrhages.

**ANGINA PECTORIS.**<sup>\*</sup> In almost every case of paroxysmal heart pain aminophylline can be depended upon to give relief no matter how acute the attack, and even when true coronary embolism appears to be the cause.—J. F. Quigley, *Prescriber*, 1935, 205.

Studies on a group of 100 patients with angina pectoris receiving either 15 to 60 gr. daily of theobromine, or 9 to 12 gr. daily of aminophylline, showed that the xanthines exert no useful specific action on cardiac pain. The patients were unable to distinguish between the effects of a xanthine and those of a placebo of lactose.—H. Gold, N. I. Kwit and H. Otto, *J. Amer. med. Ass.*, i/1937, 2173.

**ASTHMA.** Aminophylline in doses of 0.48 g. diluted to 10 ml. with saline or glucose solution, and introduced slowly intravenously, seems to be a most effective, prompt, safe and reliable therapeutic procedure for the combating of status asthmaticus even after refractoriness to adrenaline has developed. Of 41 injections given in 16 clinical cases 31 afforded prompt, complete and persistent relief.—G. Herrmann and M. B. Aynesworth, *J. Lab. clin. Med.*, 1937, 23, 135.

Successful results obtained by intravenous injections in adrenaline-resistant asthmatics. The contents of a 10 ml. ampoule, containing 0.24 g. of aminophylline are injected very slowly in cases in which repeated doses of adrenaline fail to relieve the attack within a few hours.—C. Hyman, *Med. Rec.*, 1939, 150, 279.

**CARDIAC FAILURE.** It has been definitely shown that theophylline with ethylenediamine, given intravenously in doses of 0.48 g. in 30 ml. of normal saline, has a favourable influence on the dyspnoea of cardiac failure, and on bronchial obstruction both in bronchial asthma and cardiac failure.—J. A. Greene *et al.*, *J. Amer. med. Ass.*, ii/1937, 1712.

**CHEYNE-STOKES BREATHING.** Euphyllin has a striking action in abolishing Cheyne-Stokes breathing, whereas theophylline alone has no effect. The effect of Euphyllin is due mainly to its ethylenediamine component, but Euphyllin may sometimes act when ethylenediamine fails. The effect is produced by a direct stimulation of the medullary respiratory centres and it occurs in the absence of any demonstrable changes in the circulation.—O. A. S. Marais and J. McMichael, *Lancet*, ii/1937, 437.

**Carena** (Continental Laboratories, London). Tablets containing 0.1 g. of aminophyllin.

**Glucophyllin** (Richter, London). Theophylline 2% in 5 ml. of 10% glucose solution. *Dose.*—5 ml. intravenously daily. Arteriosclerosis, cardiac decompensation, and pneumonia.

**Glucophylline** (Abbott Laboratories, London). Tablets containing theophylline 1.18 gr. and methyl glucamine 1.16 gr. Coronary dilator and diuretic for use in coronary disease and cardiac decompensation.

In both anaesthetised dogs and normal human beings Glucophylline acted as a good diuretic, exhibiting an action superior to caffeine but similar to the other salts of theophylline. It has a longer duration of action than aminophylline.—A. H. Maloney, A. F. Burton and J. W. L. Robinson, *J. Lab. clin. Med.*, 1937, 22, 600.

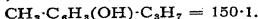
**Bassia** (B.P.C.). *Syn.* MOWRAH, MOWRA, ILLIPE.

The seeds of *B. latifolia*, *B. longifolia* and *B. butyracea*, containing 50 to 55% of a semi-solid pale yellow fixed oil with unpleasant taste and odour. When bleached by light and air the product is mowrah butter (illipe butter), used as food in India and for the manufacture of chocolate. The powdered cane remaining

after expression of oil is mowrah meal. It contains the poisonous saponin, mowrin, and is used as a worm-killer for lawns (4 oz. per sq. yard). The hardened fat is used in margarine manufacture.

## THYMOL

B.P., U.S.P. XI, P. *Helv.* V, Fr. *Cx.*, P. Belg. IV, P. Ital. V.



Syn. ACIDO TIMICO (F.E. VIII), 3-METHYL-6-ISOPROPYLPHENOL.

**Dose.**— $\frac{1}{2}$  to 2 grains (0.03 to 0.12 g.), in pills with soap and a trace of alcohol, or in oily or aqueous solution. *Anthelmintic dose.*—15 to 30 grains (1 to 2 g.). U.S.P. XI states 30 gr. divided into 3 doses. F.E. states maximum in 6 hours 1 to 2 g. It is best given finely powdered and mixed with sodium bicarbonate or lactose to prevent agglomeration of the particles.

Occurs in colourless crystals with characteristic pungent odour and taste. Prepared synthetically from piperitone obtained from the oil of *Eucalyptus dives* or extracted from oils of thyme, *Monarda punctata*, or ajowan, *Trachyspermum Ammi*.

Oil of thyme contains 20 to 30% of thymol, *Monarda punctata* oil contains about 60%, and ajowan oil 45 to 55%.

**Soluble** 1 in 1500 of water, 1 in 200 of glycerin, 1 in 8 of alcohol and glycerin, equal parts; soluble in fats and oils, and 8 in 3 of alcohol 90%, and freely soluble in ether, acetic acid and caustic alkalis. Liquefies with menthol, chloral hydrate, camphor and phenol.

**Uses.** Thymol is a more powerful antiseptic than phenol, but the local effects and the toxicity are relatively slight because of its low solubility and slow absorption. Large doses internally irritate the mucosa of the stomach and small intestine and after absorption produce tinnitus, headache, vomiting and collapse.

Almost its only use internally is in the treatment of ankylostomiasis. For this purpose it is customary to give the drug in two divided doses of 30 gr. each. The preparation of the patient is important and the following procedure is recommended. The patient is given a light meal and a saline purgative the night before. At 8.30 the following morning 30 gr. of powdered thymol is given in capsules; at 10 a.m. another similar dose is given, and at 12 a saline purgative. No food or alcohol is permitted until the bowels have moved. The treatment may be repeated in a week if necessary. In pregnant women, or cases of very bad infection, and in elderly patients, or those with heart disease or extreme debility, the dose is 30 gr. or less in divided doses. For children the doses are proportionately less. Thymol is also stated to have given good results, in similar dosage, in actinomycosis.

Externally, thymol is a powerful parasiticide and is used as a paint or ointment in the treatment of ringworm, eczema and other skin diseases. A 5% alcoholic solution has been used in place of tincture of iodine for sterilising the skin prior to operation.

A 1 in 2000 solution makes a pleasant and efficient antiseptic gargle or mouth-wash, and may also be used for spraying the nasal mucous membrane in catarrhal conditions.

**ACTINOMYCOSIS.** Thymol used with excellent results. The method consists in giving orally 1·5 g. of powdered thymol in capsules two days out of three; all sinuses are opened widely and curetted and filled with thymol in olive oil (10% solution). The sinuses are injected each day until they heal from the bottom.—Joyce, per *Med. Pr.*, 1939, 213.

**ANKYLOSTOMIASIS.** The dangers of thymol are overrated, but untoward effects in patients with chronic disease of the intestine and in œdematous patients. Most effective on hookworms, but usually fails to remove heads of tapeworms.—R. N. Chopra and A. C. Chandler, *Anthelmintics and Their Uses* (Ballière, Tindall & Cox, 1928).

Thymol was in greatest use when prolonged examination aimed at, and must often have succeeded in disclosing, deworming. For successful use it must be particulated. Thymol crystals readily set into a solid mass, so that when packed into a digestible capsule its shape may still be recognised in the bare lump of wasted thymol passed in the faeces. Two courses, each of 60 gr. of "finely particulated" thymol, will effect deworming in about 50% of adults. Moreover, such deworming is safe in those not already moribund or nearly so. Howard (1919) pointed out how persistently it was stated that 60-grain adult doses of thymol were dangerous, but there had actually been given over a million such doses in the United States with no death. Actually, thymol is as safe as it is because, like alcohol, it is apt to produce early symptoms of intoxication, and the intoxicating dose is far removed from that which kills. Methods of drug appraisalment of the treatment of hookworm seem to leave thymol in the first place when safety and efficiency are both considered.—C. Lane, *Lancet*, i/1935, 1461.

**Gargarisma Antisepticum (Mid. H.).**

Boric acid 6 gr., thymol  $\frac{1}{2}$  gr., oil of eucalyptus  $\frac{1}{2}$  m., oil of peppermint  $\frac{1}{2}$  m., glycerin 24 m., fuchsine q.s., water to 1 oz. A useful general gargle.

**Glycerinum Thymolis Compositum (B.P.C.).**

*Syn.* GLYCERINUM THYMOL ALKALINUM.

A solution containing sodium bicarbonate, borax, sodium salicylate, menthol and thymol with other aromatic antiseptics.

Moulds and bacteria will grow in this preparation even when undiluted. The germicidal powers of the dilutions usually employed must be negligible.—F. J. Bolton and R. W. Richardson, *Pharm. J.*, i/1936, 117.

**Hartman's Solution.** Thymol  $1\frac{1}{2}$  parts, ethyl alcohol 1 part, ether 2 parts (all by weight). Applied on a pledget of cotton-wool directly to the dentine it desensitises the pulp for from 20 minutes to an hour, thus allowing of the preparation of the cavity for filling.—per *J. Amer. pharm. Ass.*, 1936, 80.

**Liquor Thymolis Compositum (B.P.C.).**

*Syn.* LIQUOR ANTISEPTICUS.

Contains boric and benzoic acids, thymol and eucalyptol with other aromatic antiseptics.

N.B. Distinguish from Liquor Antisepticus (N.I.F.), see page 468.

**Mistura-Oleo-Balsamica.** *Syn.* BALSAMUM VITÆ HOFFMANNI, "TINCTURE OF LIFE." *Dose.*—1 to 4 drachms in water.

Oils of lavender, thyme, lemon, nutmeg and orange-flowers, of each 4; oil of clove and cinnamon of each  $3\frac{1}{2}$ ; balsam of Peru 10½; alcohol 90% to 1000; allow to stand a few days, then filter.

A remedy for snake bites. A carminative stimulant.

**Pigmentum Thymolis.**

Thymol 1, ether 10, and alcohol 90% 5; used as pigment in ringworm of the scalp—whilst acting as parasiticide it dissolves the fat, loosens the hairs and thus helps epilation.  $2\frac{1}{2}$  to 5% in a mixture of chloroform and olive oil is also used.

**Sapo Thymol (St. G. H.).**

Thymol 5 gr., soft soap  $\frac{1}{2}$  oz., alcohol 90% to 1 oz.

**Volckmann's Thymol Solution.**

Thymol 1, alcohol 90% 20, glycerin 20. Dissolve and add to water 00. Used as a spray and antiseptic lotion, e.g., for burns.

**Unguentum Thymolis.**

Thymol 20 gr., soft paraffin to 1 oz. Dissolved by heat. Used in the later stages of eczema and for other skin affections. Applied half strength to the skin keeps off gnats, etc.

**Vapor Thymol (T. H.).**

Thymol 6 gr., alcohol 90% 1 dr., light magnesium carbonate 3 gr., water to 1 oz. A teaspoonful to a pint of water at 140°F. for inhalation. A strong stimulant.

**Angicid (Richter, London).** Mouthwash tablets containing thymol, menthol, caryophyllum and peppermint oil.

**Borol (Parke, Davis, London).** Borate, bicarbonate and benzoate of sodium with eucalyptol, menthol, oil of pine, etc. For use as a gargle, mouthwash and spray, or for vaginal injection.

**Eubrol (Parke, Davis, London).** Euthymol and fluid extract of red gum. Mouthwash.

**Euthymol (Parke, Davis, London).** Eucalyptol, oil of wintergreen, menthol, thymol, benzoic acid and boric acid. Liquid mouthwash, gargle, etc.

**Glycethymoline Brand Solution (Kress & Owen, New York; Christy, London).** "Borax 2.010, thymol 0.037, orcelli 0.123, menthol 0.037, benzol hydrate 1.68, Ol. Betule Lentæ 0.030, Sod. acid carb. 2.346, S.V.R. 4.085, glycerin 16.749, cajeputol 0.075, distilled water 72.708, Hyd. Oxybenz. 0.074, Ol. Pumi Ess. 0.037."

**Thymaglycine (Martindale, London).** Antiseptic solution containing sodium benzoate, glycerin, menthol, essential oils, and thymol. As such, or diluted, is beneficial in rhinitis, pharyngitis, quinsy, and in gastric and intestinal catarrh. *Dose*.—10 to 30 minims (0.6 to 2 ml.).

**Zymocide (Reed & Carrick, New Jersey; Coates & Cooper, London).** Antiseptic germicide containing thymol, eucalyptol, menthol, methyl salicylate, boric and benzoic acids. For use as a spray, gargle and mouthwash and for local application.

**Thymolis Iodidum (B.P.C., U.S.P. XI).**

*Syn. and Prop. Name.* DITHYMOL DIODIDE, ARISTOL (Bayer Products, London).  $(C_6H_2(CH_3)(C_3H_7)OI)_2 = 550.0$ .

Reddish-brown or brick-red powder with slight aromatic odour; almost tasteless. Contains not less than 40% of I.

**Insoluble** in water, alcohol, glycerin, sodium hydroxide solution; soluble almost completely 1 in 10 of ether, also 1 in 50 of chloroform and in collodion, soft paraffin and fixed and volatile oils.

**Incompatible** with alkalis, mercuric chloride, metallic oxides or anything decomposing iodides.

**Uses.** Thymol iodide is used as an iodoform substitute, since it has the advantage of being practically odourless. It has, however, only weak antiseptic properties and does not liberate iodine in the tissues, and it cannot therefore replace iodoform in surgery. It is employed as a dusting powder for burns or wounds, as an ointment (2 to 10%) in psoriasis, eczema, etc., and as a 3% ointment made with soft paraffin for use in ozæna.

**Thymi Herba (B.P.C., P. Helv. V, Fr. Cx.).**

The dried flowering tops of thyme, *Thymus vulgaris* (Labiatae).

**Elixir Thymi (B.P.C.).**

*Dose*.—1 to 2 drachms (4 to 8 ml.).

Contains ammonium bromide 2 gr. and liquid extract of thyme  $7\frac{1}{2}$  m. per dr. with spirit of chloroform, glycerin, treacle and syrup. For whooping cough.



**Extractum Thymi Liquidum (B.P.C.).** *Syn.* EXTRACTUM THYMI VULGARIS LIQUIDUM. *Dose.*—10 to 60 minims (0.6 to 4 ml.). 1 in 1.

**Syrupus Thymi.**

Liquid extract of thyme 1, syrup 7. *Dose.*—1 to 4 drachms (4 to 16 ml.).

**Oleum Thymi (B.P.C.).**

*Dose.*—1 to 5 minims (0.06 to 0.3 ml.).

Distilled from the fresh herb. A dark reddish-brown liquid containing not less than 40% of phenols (thymol and carvacrol). Used in whooping cough and bronchitis, and externally as a rubefacient.

"Red" thyme oil on rectifying is converted into white thyme oil, which contains 20 to 30% of phenols. Spanish thyme oil is probably derived from a species of *Origanum*.

**Oleum Ajowan (B.P.C.).** *Syn.* PTYCHOTIS OIL. *Dose.*— $\frac{1}{2}$  to 3 minims (0.03 to 0.2 ml.). The oil distilled from the fruits of *Trachyspermum Ammi*, containing not less than 40% of thymol. Used in India as a carminative.

**Oleum Majoranae**, from *Origanum majorana*, contains practically no phenols.

**Oleum Origani**, from *O. hirtum* and *O. majoranoides*, may contain up to 85% of carvacrol.

**Karvol** (Crookes Laboratories, London). A mouthwash and gargle containing chlor-carvacrol as a basis. Also prepared as a dental cream, inhalant, liniment, insect-bite lotion, etc.

## THYROIDEUM

*B.P., U.S.P. XI, Fr. Cx., etc.*

*Syn.* THYROIDEUM SICCUM, DRY THYROID, THYROID EXTRACT, THYROID GLAND, THYROIDINE (P. Belg. IV).

[P1] "*Thyroid gland, the active principles of; their salts.*"

[S6] "*Thyroid gland, the active principles of; their salts—specify proportion as either*

(a) *the proportion of thyroid gland contained in the preparation;*  
or

(b) *the amount of thyroid gland from which a specified quantity of the preparation was obtained together with an indication whether the amount relates to fresh or to dried gland.*"

[S7] *Medicines made up ready for the internal treatment of human ailments containing—Thyroid gland, the active principles of; their salts—must be labelled with the words "Caution. It is dangerous to take this preparation except under medical supervision."*

*Dose.*— $\frac{1}{2}$  to 5 grains (0.03 to 0.3 g.).

For methods of assay and notes on iodine content see Vol. II.

In view of the increasing demand for 5-grain tablets of thyroid extract, it should be realised that the *B.P.* preparation "Thyroideum," is five times as strong as the fresh gland preparation. Complaints from doctors and chemists of untoward effects following the use of 5-grain thyroid tablets showed on enquiry that fresh gland was intended to be used. Unless fresh gland is specifically asked for there is almost a certainty of the stronger extract being supplied.—*Brit. med. J.*, i/1934, 1039.

Obtained from the thyroid glands of ox, sheep and pig. After removal of connective tissues and external fat the glands are dried below 60°, powdered, and fat extracted by light petroleum. The product is diluted with lactose to contain 0.09 to 0.11% of iodine in combination as thyroxine.

The thyroid gland is situated in the neck and consists of two lobes, one on each side of the upper part of the trachea and larynx, joined by an isthmus. In man the gland weighs about 25 grammes and the average length of each lobe is 2 inches. It is larger in the female than in the male. One lobe ( $\frac{1}{2}$  gland) of the sheep's thyroid weighs on an average about 35 grains and yields about 9 grains of dry thyroid. Histologically the thyroid has an external capsule of dense connective tissue which sends trabeculae into the interior, dividing it into irregular lobules. The lobules consist of groups of closed oval or spherical vesicles connected by areolar tissue and lined by a single layer of columnar epithelium. The vesicles contain a yellow viscid fluid called colloid.

The gland normally contains about 10 or 15 mg. of iodine. Four iodine-containing compounds may be obtained from the gland—thyroxine, diiodotyrosine, diiodothyronine and iodothyroglobulin. (Diiodotyrosine has been used in the treatment of hyperthyroidism, but its effects would appear to be no different from those of iodine in other forms. Diiodothyronine has been used in myxœdema, the effect of 50 mg. of the disodium salt being equivalent to that of 1 mg. of thyroxine). Opinion is changing to the view that total iodine is a better guide to activity than thyroxine iodine.

The active substance liberated into the blood stream is not thyroxine. It may possibly be a peptide containing thyroxine and diiodotyrosine linked together directly or through other amino-acids. On this theory, artificial breakdown of thyroglobulin ruptures the linkage leaving residual activity in the thyroxine fraction only, whereas natural breakdown, which constitutes the normal release of active secretion, consists in the liberation of the intact peptide containing both thyroxine and diiodotyrosine.—C. R. Harington, *Brit. med. J.*, ii/1936, 1271.

**Physiology.** The principal function of the thyroid gland is to increase oxidation processes in the body; thus all body activities are influenced by the state of the thyroid. Deficiency of thyroid secretion results in a fall in heat production—*i.e.*, decrease in the rate of metabolism and general loss of mental and physical vigour. The pulse is slower, the skin becomes dry and thickened in the subcutaneous layers. Congenital thyroid deficiency leads to the condition of cretinism, characterised by poor mental and physical development. Deficiency in the adult results in the condition termed myxœdema. Excess of thyroid secretion increases the basal metabolic rate, body tissues are burned up with the result that the individual becomes thin. Mental activity is increased and the rate of the heart beat is quickened.

The functioning of the thyroid gland is intimately related to the amount of iodine in the diet—deficiency of iodine leads to enlargement of the thyroid, as seen in endemic goitre. Diets rich in protein and fats increase the rate of discharge of thyroxine from the gland and lead to enlargement. Rickets-producing diets (*i.e.*, diets low in phosphorus and high in calcium or *vice versa*) cause thyroid enlargements in dogs and cats if the iodine intake is low.

The activity of the thyroid gland is influenced by the action of other endocrine glands in the body. The anterior lobe of the pituitary gland contains a thyroid-stimulating or thyrotropic substance which can be extracted by aqueous alkali. Removal of the thyroid gland from animals leads to enlargement of the anterior

pituitary. Persons with large parenchymatous goitres have enlarged anterior pituitaries. The thyroid and pituitary glands are delicately balanced. Any deficiency in the thyroid secretion quickly stimulates the pituitary, either directly or by way of a nervous mechanism, to produce more thyrotropic hormone. Conversely, supplying the thyroid hormone reduces anterior pituitary activity.

Enlargement of the thyroid occurs during menstruation and pregnancy; this fact, together with the frequency of goitre at puberty and the menopause, suggests a relationship of thyroid function with that of the gonads. Removal of the gonads from animals results in a depression of thyroid function. Administration of thyroid has an inhibitory effect on oestrus. Contradictory results on thyroid activity have been reported from the administration of oestrin; some workers report increased thyroid activity, others the opposite effect. The influence of the thyroid on the gonads is probably exerted through the medium of the anterior pituitary.—D. Marine, *J. Amer. med. Ass.*, i/1935, 2253.

### Tests for Thyroid Activity

**BASAL METABOLIC RATE (B.M.R.)** means the rate of energy exchange in the body as seen under basal conditions (after elimination of movement, digestion, etc.). A relatively simple way of determination (as described by Benedict, *J. Amer. med. Ass.*, ii/1921, 247; and Krogh, *Brit. Ass. Rep.*, 1921, 445) is to measure the oxygen consumption of the patient during a given period. Oxygen is rebreathed in a closed-circuit apparatus in which the exhaled  $\text{CO}_2$  is absorbed; the diminution in volume of the gas indicates the amount of oxygen consumed. The B.M.R. does not vary as much as 10%. In hyperthyroidism it rises to 25 or 50% above normal, or even more; while in deficiency the rate falls below normal.

Determination and interpretation.—H. F. Moore, *Lancet*, i/1925, 219. See also J. D. Robertson, *Practitioner*, ii/1935, 780.

There is a steady increase in the rate during infancy from the low values of approximately 25 calories an hour per square metre of body surface obtained on new-born infants to a maximum value somewhat greater than 50 calories an hour per square metre at an age of between 3 and 5 years. Thereafter a gradual decrease in basal metabolism occurs during childhood, middle age and old age.—*J. Amer. med. Ass.*, ii/1936, 357.

**Goetsch's Adrenaline Test** depends upon the fact that the sympathetic nervous system in cases of hyperthyroidism is specially sensitive to adrenaline. Blood pressure, pulse rate and respiration rate are recorded at intervals after the subcutaneous injection of 0.5 ml. of adrenaline chloride solution. A rise of blood pressure, with an increased pulse and respiration rate, is considered diagnostic of hyperthyroidism.

**THE "IMPEDANCE ANGLE"** as a test for the diagnosis of diseases of the thyroid gland. In constant-current work the impedance of the body (i.e., resistance due to self-induction) is measured by a single factor, namely, the resistance; but with alternating currents the body functions as a condenser as well. It is the ratio of these two factors, termed the impedance angle (I.A.), which shows variations in disease of the thyroid. The author describes a comparatively simple apparatus which gives direct readings of this value. The patient, seated in a chair, has each arm immersed in a 10-litre bath of 1% saline at 25°. Alternating current of low intensity is passed through the patient into a simple bridge circuit. The impedance offered by the body is balanced on the bridge by adjusting a variable resistance and condenser. The impedance angle is increased in thyrotoxicosis; in non-toxic goitres it is generally lower than normal. This test is claimed to be more specific and certain than B.M.R. determination.—M. A. B. Brazier, *Lancet*, ii/1933, 742. See also *J. Instn. elect. Engrs.*, 1933, 203.

**Estimation of blood cholesterol** as a guide to thyroid therapy. Creatinuria occurs before any change in B.M.R. is noted, and is a delicate index of the effect of thyroid treatment.—J. E. Hess, *Ann. Int. Med.*, 1934 (Nov.), 607. Also Gilligan, *ibid.*, 1934, (Nov.), 84, 746.

**Iodine tolerance test of value in diagnosis of a typical hypothyroidism.**—A. W. Elmer, *Endocrinology*, 1934, 487.

**Quinine Test.** From a series of more than 4000 cases it appears that the quinine test for thyrotoxiæmia is a dependable guide in diagnosis, the frequency of error not exceeding 5%. The tolerance for quinine in hyperthyroidism appears to vary in direct proportion with the height of the basal metabolism rate, and is fairly parallel with it, serving as a guide to progress under treatment. Depending on the severity of active hyperthyroidism, patients are able to take 30 grains or more of quinine sulphate or hydrobromide daily for weeks without evidence of cinchonism. It is as dependable as the basal metabolic rate and as accurate a guide in treatment. It does not discriminate between toxic adenoma and exophthalmic goitre.—*J. Lab. clin. Med.*, 1935, 21, 123.

**Toxic Effects.** Over-doses of thyroid preparations may cause rapid pulse, "racing" of the heart, feverishness, headache, pruritus, and even delirium. Chronic thyroid poisoning has also been observed—the symptoms being emaciation, muscular weakness, loss of hair, dilated pupils and general debility.

Very rarely the administration of thyroid extract for the treatment of myxœdema, the relief of obesity, or some other purpose, is followed by the development of exophthalmos, and an example of this is reported. It is probable, therefore, that when exophthalmos follows the administration of thyroid extract, this is not a direct result of the action of the thyroid extract, but is due to some other substance which in certain rare individuals is produced in response to thyroid extract. Experimental evidence suggests that the substance may be the thyrotropic hormone of the pituitary.—W. Russell Brain, *Lancet*, i/1936, 186.

**Thyroid Addiction.** Details of three cases of thyroid addiction. The symptoms of excessive intake were loss of weight, fall in blood pressure, excitement and other indications of thyrotoxicosis. Keogh points out that the administration of thyroid hormone in sufficiently large amounts leads to a thyrotoxic condition resembling in many ways exophthalmic goitre.—S. W. Patterson, *Brit. med. J.*, ii/1934, 6.

**Uses.** Thyroid exerts a powerful effect on metabolism. Administered by the mouth, it increases energy, improves the appetite and brightens the mental outlook. The most striking results of thyroid treatment are in cretinism and myxœdema, doses of  $1\frac{1}{2}$  to 2 gr. daily being sufficient to produce dramatic improvement, though it is necessary in most cases for the patient to continue taking thyroid for the rest of his life. Owing to its marked action in stimulating the general metabolism thyroid treatment is often strikingly effective in obesity, especially in that developing at the menopause, but the results are not permanent and great care must be taken to avoid overdosage. Apart from its specific indications, thyroid is widely prescribed as a general tonic in neurasthenia, convalescence and fatigue; for this purpose it should be prescribed in doses of  $\frac{1}{2}$  gr. twice daily for a period not exceeding a fortnight at a time. Thyroid is also beneficial in young children who are making little physical and mental progress, and in women between the ages of 18 and 35 who appear to be suffering from a minor degree of thyroid deficiency, as evidenced by loss of appetite, loss of energy and amenorrhœa. It is also of value in dysfunctional menstrual disorders, especially when associated with a low metabolic rate.

Thyroid medication has been employed as a non-specific metabolic stimulant in numerous conditions, such as arthritis, psoriasis, senile eczema, indolent ulcers, etc., but the results are too inconstant for the treatment to be of appreciable value.

Following large doses there is increased excretion of water by the kidneys, and beneficial results may sometimes be obtained from its use in nephrosis.

**CRETINISM.** As soon as cretinism is recognised or even suspected treatment should be started. Thyroid should be given in very small doses at first and increased rapidly, if it is well tolerated. It is best to begin with  $\frac{1}{16}$  gr. twice daily, and after three days give it three times a day. Then the dose is increased every week until  $\frac{1}{2}$  gr. is given three times daily. Improvement is rapid and should be very obvious in three or four weeks. The optimum dose varies. There should be a steady gain in weight, regular action of the bowels, and no disturbance in general health. Loss of weight and diarrhoea are the two most useful indications of overdosage. Occasionally a baby is very intolerant even of the smallest dose, and with every increase much loss of weight, diarrhoea and general disturbance of health take place. In such cases it is necessary to proceed with extreme caution, allowing the child time to recover the lost weight and add a little more before any further increase in the dose is made. Thyroid must be administered without intermission and as soon as a child is old enough to co-operate it is useful to have an estimation of the basal metabolic rate. In general the earlier treatment is begun the better the outlook, and it is for this reason that early diagnosis is so important. It is true that so long as treatment has been started in the first year or two the physical signs of cretinism disappear entirely, but the effect on the mental development is much less satisfactory. Even in babies who have had an adequate dose of thyroid from the second or third month onwards the result is sometimes most disappointing and the intelligence may be subnormal or even abnormal. The majority always remain a little below the average in mentality, but some respond so well that they become indistinguishable either mentally or physically from normal people of their own age. Even in the case of cretins treated for the first time between the ages of one and three years the response is sometimes unexpectedly good. If, however, the treatment is not instituted until the later years of childhood neither the appearance nor the mentality ever becomes normal, though the improvement in looks and height may be considerable.—E. A. Cockayne, *Practitioner*, ii/1935, 767.

**MENSTRUAL DISORDERS.** Desiccated thyroid extract is a most effective weapon in the treatment of dysfunctional menstrual disorders. Acting as a specific agent, thyroid extract promptly alleviates the menorrhagia of hypothyroidism which is often the cause of hæmorrhages in adolescent girls. It is also of value when employed empirically as a non-specific adjunct in therapy, because of its augmentation of all cellular activity. The toxicity of overdosage may be avoided by observing two principles: (a) The initial dose should be small ( $\frac{1}{4}$  gr. thrice daily) irrespective of the B.M.R. The amount administered should be increased rapidly to the point of tolerance, and the maintenance dose continued at a slightly lower level. (b) Accurate dosage should be ensured by always employing the same brand of extract.—S. L. Israel, *Endocrinology*, Feb. 1938, 253.

**MYXEDEMA.** In fully developed cases an initial dose of 1 gr. may be increased to 2 or 3 gr. and continued until the symptoms have disappeared. Then a maintenance dose of 1,  $1\frac{1}{2}$ , or 2 gr. daily is all that will be required during the second stage to keep the patient free from symptoms of hypothyroidism for the rest of his life. The dose should be reduced in hot weather and during the course of an acute febrile disease.—G. R. Murray, *Practitioner*, i/1938, 2.

**ULCERS** in the leg quickly healed under thyroid treatment (2 gr. t.i.d.) in a few weeks although they had not changed under other treatment for six years.—M. H. Cohen, *J. Amer. med. Ass.*, i/1934, 283.

[P1-87] **Soluté Injectable de Glande Thyroïde (Fr. Cx.).** It contains in 100 ml. the active principles equivalent to 10 g. of fresh thyroid.

[P1-87] **Tab. Mixed Gland (Male) (D.T.F.).** Pituitary (whole gland), supra-renal, didymin, thymus and thyroid glands, of each  $\frac{1}{16}$  gr. per tablet. [P1-87] **Tab. Mixed Gland (Female) (D.T.F.)** are similar but contain mammary and ovarian glands, of each  $\frac{1}{16}$  gr., in place of didymin.

#### SOME PROPRIETARY THYROID PREPARATIONS

[P1-87] **Anobese (Paines & Byrne, London).** Thyroid, anterior pituitary, thymus, ovary (or testes), and lymphatic substance. Capsules or ampoules ("M" or "F"). *Dose.*—3 to 6 capsules daily with 2 or more injections weekly. Obesity of the "water-logged" type.

[P1-87] **Cavolysin** (*Cavendish Chemical Co., London*). Contains thyroid, anterior pituitary, thymus and testicular substance; for women, the testicular substance is replaced by ovarian. Supplied in tablets and in ampoules for intramuscular injection. For obesity.

[P1-87] **Elityran** (*Bayer Products, London*). Biologically standardised thyroid extract tablets ( $\frac{1}{2}$  gr. = 10 guinea-pig units) and ampoules (8 g.p. units). *Dose*.—1 or 2 tablets thrice daily, or 0.5 ml. intramuscularly daily, increased to 2 ml. Obesity, thyroid insufficiency, etc.

Production of Elityran outlined. Two iodine-containing protein fractions are separated from the thyroprotein by precipitation with saturated ammonium sulphate solution and dialysed.—*Endocrinology*, 1933, 13, 250.

[P1-87] **Endothylin** (*Endocrines-Spicer, Watford*). Each tablet contains  $\frac{1}{2}$  gr. of desiccated thyroid with magnesium phosphate, calcium phosphate (dibasic) and glycerophosphate, and potassium and sodium bicarbonates.

[P1-87] **Glandiposan** (*Richter, London*). Tablets of thyroid B.P.  $\frac{1}{2}$  gr. and anterior pituitary  $\frac{1}{2}$  gr. *Dose*.—1 tablet thrice daily. For obesity.

[P1-87] **Glandiposan Forte** tablets contain thyroid 3 gr. and anterior pituitary  $\frac{1}{2}$  gr. *Dose*.—1 thrice daily.

[P1-87] **Hormonigen Tablets** (*Hewlett, London*). Contain thyroid, pituitary, ovary and testis. *Dose*.—1 or 2 tablets before meals. In neurasthenia and for pluriglandular therapy.

[P1-87] **Hormotone** (*G. W. Carnrick, Newark, N.J.; Brooks & Warburton, London*). A combination of hormones derived from the thyroid, pituitary, gonad and suprarenal glands. Each tablet contains  $\frac{1}{2}$  gr. of desiccated thyroid and pituitary. *Dose*.—One or two tablets thrice daily before meals; not more than six per day. Stated to increase mental, nerve, and muscular activity. Also available without post-pituitary.

[P1-87] **Incretone** (*G. W. Carnrick, Newark, N.J.; Brooks & Warburton, London*). Contains thyroid, pituitary and gonads. *Dose*.—1 to 2 teaspoonfuls before meals. For use in asthenia, general debility, etc.

[P1-87] **Iodobesin** (*Anglo-French Drug Co., London*). Tablets containing hepatic, pituitary, orchitic, ovarian, thyroid (deprived of lipoids), and suprarenal extracts, and Iodalbumin. For obesity.

[P1-87] **Neolydin Tablets** (*Endocrines-Spicer, Watford*). Each tablet contains whole adrenal gland  $\frac{1}{2}$  gr., Endothylin  $\frac{1}{2}$  gr., pituitary (anterior lobe)  $\frac{1}{2}$  gr., prostate  $1\frac{1}{2}$  gr., lydin ("a concentrated testicular desiccation prepared from the interstitial cells of Leydig")  $1\frac{1}{2}$  gr., with magnesium phosphate, calcium gluconate and glycerophosphate, and sodium and potassium bicarbonates to 6 gr. In impotence, neurasthenia, etc. *Dose*.—1 tablet thrice daily, increasing to 2 or 3 thrice daily.

[P1-87] **Paromin** (*Paines & Byrne, London*). Preparation of thyroid standardised on its calorific activity, containing not less than 0.5% of natural organic iodine. In  $\frac{1}{2}$ -grain tablets and 1 ml. ampoules (5 gr. of fresh substance).

[P1-87] **Protonuclein** (*Reed & Carnrick, Jersey City; Coates & Cooper, London*). Tablets containing thyroid, suprarenal, lymphatic gland, brain, spleen, pancreas, thymus, with pepsin, salivary glands and excipients.

[P1-87] **Sembo** (*Napp, London*). Mixed gland tablets containing extracts of thyroid, thymus, pituitary (anterior), suprarenal and cerebrian, and orchis, with calcium glycerophosphate and phosphate of iron. Asthenia, impotence and premature senility. [P1-87] **Flatal** tablets for women contain in addition extracts of ovary and mammary gland.

[P1-87] **Tetraglandular Tablets** (*Parke, Davis, London*). Desiccated suprarenal, pituitary, thyroid and parathyroid glands. *Dose*.—1 or 2 tablets.

[P1-87] **Thyracoids** (*Reed & Carnrick, New Jersey; Coates & Cooper, London*). Desiccated thyroid tablets.

[P1-87] **Thyrafar Tablets** (*Parke, Davis, London*). Desiccated thyroid gland, desiccated suprarenal gland and Bland's pill. *Dose*.—1 tablet twice or thrice daily.

[P1-87] **Thyranon** (*Organon Laboratories, London*). Thyroid extract standardised chemically to 0.2% total iodine, and biologically.

[P1-87] **Thyrin** (*Richter, London*). A preparation of fresh thyroid gland substance for injection, 1 ml. containing 10 gr. of fresh thyroid extract. *Dose*.—1 ml. intramuscularly.

[P1-87] **Thyroidin Elixir** (*Allen & Hanburys, London*). Contains the equivalent of 5 gr. of fresh thyroid in each dr. *Dose*.—1 to 4 drachms.

[P1-87] **Thyroprotein** (*Beebe*) (*Parke, Davis, London*). A standardised, concentrated extract, consisting of the pure proteid of healthy thyroid gland without the undesirable accompaniments often present in commercial varieties of the dried gland. Standardised to contain 0.33% of organically combined iodine. Tablets weigh 2 gr. each and contain  $\frac{1}{10}$  gr. of the thyroid proteid. *Dose*.—One tablet. Also supplied in ampoules containing Thyroprotein  $\frac{1}{20}$  gr., and Chloretone  $\frac{1}{15}$  gr., in 1 ml. for hypodermic injection.

[P1-87] **Thyroxinsodium** (*B.P.*).  $C_{15}H_{10}O_4NI_4Na = 776.8$ .

*Dose*.— $\frac{1}{100}$  to  $\frac{1}{4}$  grain (0.0001 to 0.001 g.). It is usually given by intravenous injection. The *B.P.* states that when thyroxine is ordered, thyroxinsodium may be dispensed.

The amount should be determined with reference to the B.M.R. It is calculated that 1 mg. of thyroxine causes an average increase of 2.8% in the B.M.R.

In patients previously treated with desiccated thyroid 1 mg. of synthetic thyroxine produces action analogous to that of 0.2 g. of the dried gland. The initial dose of thyroxine in the adult should not be more than 0.5 mg.

With a myxoedematous patient the maximum effect is produced on the tenth day after a single injection.

A person afflicted with high-grade myxoedema requires from 1.5 to 2 mg. per day, and a small cretin from 0.2 to 0.4 mg. every day or every other day.

Thyroxinsodium is the monosodium salt of thyroxine, which is *dl*- $\beta$ -[3 : 5-diiodo-4(3' : 5'-diiodo-4'-hydroxyphenoxy) phenyl]- $\alpha$ -aminopropionic acid. It contains 61 to 65% of I, and occurs as a white, crystalline powder, obtained by the action of a limited amount of sodium carbonate on thyroxine, which may be prepared synthetically or extracted from thyroïd gland.

Sparingly *soluble* in water, more soluble in aqueous alkalis, forming unstable solutions.

Thyroxine prepared from casein and iodine was reported by Ludwig and Mutzenbecher (*Hoppe-Seyl, Z.*, 1939, 258, 195). This has been confirmed in every respect. The experiments must be conducted under very carefully controlled conditions, when the yield obtained approximates to 100 mg. of thyroxine from every 100 g. of iodinated casein. Possible mechanisms of the reaction are advanced.—C. R. Harrington and R. V. Pitt Rivers, *Nature, Lond.*, ii/1939, 205.

**Caution.** The action of thyroxine persists for 15 or 21 days. Wait until effect has passed off before giving a further injection.

The therapeutic use of thyroxine is limited by the necessity for intravenous injection as, owing to its extreme insolubility, it is absorbed irregularly when given by the mouth.

**Uses.** Thyroxinsodium is used for the same purposes as thyroid, and is given in cretinism, myxoedema and simple goitre (but *not* in exophthalmic).

Based on the view that otosclerosis results from a diminished blood supply to the ear, owing to the gradual failure of vasomotor response, this condition has been treated by the local application of thyroxine, which causes a prolonged active congestion without inflammatory reaction.

**OTOSCLEROSIS.** The tympanic membrane is anaesthetised with a freshly prepared 10% solution of cocaine in aniline, applied for 5 minutes and the canal mopped quite dry. Thyroxine  $\frac{1}{10}$  gr. dissolved in 4 m. of water is injected into the tympanic cavity at a point midway between the tip of the handle of the malleus and the posterior margin of the membrane. A gag placed between the teeth prevents the patient from swallowing and so opening the Eustachian tube, and the head is tilted backwards for 5 or 10 minutes immediately after the

injection. In a preliminary report of 14 cases it is stated that about 50% of cases of otosclerosis and "dry middle-ear catarrh" can be greatly improved in regard to both hearing and tinnitus.—A. A. Gray, *J. Laryng.*, 1935, 50, 729.

In 30 cases treated, 4 patients showed improvement in bone conduction only, and 8 in air and bone conduction. Patients injected with histamine acid phosphate showed results as good as with thyroxine, and in 11 patients injected with normal saline only 7 showed improvement—tinnitus was relieved by saline more often than by thyroxine.—S. C. Suggitt, per *Med. Annu.*, 1937, 112. In a series of 15 cases treated by thyroxine there was definite improvement in one case and slight in 6.—T. B. Jobson, per *Med. Annu.*, 1937, 112. The results obtained are most discouraging. Suggitt is justified in concluding that the results are due to the injection of fluid into the middle-ear cavity. Some years ago temporary successes were occasionally obtained by injecting liquid paraffin and Fibrolysin into the middle ear to loosen hypothetical adhesions.—F. W. Watkyn-Thomas, *ibid.*

§ Of 42 cases treated in this manner, 23 showed definite improvement in hearing capacity, ten slight, and 9 were failures. Four consecutive thyroxine injections are given, alternately in the right and left ears at intervals of one week. A careful audiogram should be made at the beginning of treatment and a second within 2 or 3 weeks after the last injection.—M. A. Goldstein, *J. Laryng.*, 1938, 53, 444.

**HYPOCHROMIC ANÆMIA.** Thyroxine increases the reticulocyte response to reduced iron.—S. van Beurden, *Ass. méd.* 1935, 13, 116.

Injections of thyroxine increase the blood platelet count in the peripheral blood, the increase usually appearing in 24 to 48 hours after the injection, and disappearing in about 72 hours. Thyrotropic hormone produces the same effect, but its action is more protracted.—H. Zondek and Kaatz, *Brit. med. J.*, ii/1936, 387.

[P1-87] **Thyroxinum (U.S.P. XI)** is the acidic substance containing not less than 64% of I as an integral part of the molecule.

*Average dose.*— $\frac{1}{16}$  grain.

**Antihormones.** If the "hormones" are to be regarded as stimulating or exciting substances, then the "antihormones" (or "catechins" as they were originally called) may be regarded as their antagonists, whose special province is to prevent excessive effects of hormones or to modify their action. It was for long assumed that hormones, belonging as they do to the natural defences of the body, would not act as antigens, but as the result of Collip's observation that parathormone gradually loses its effect on repeated injection, the existence of antihormones has now been established. It is now known, for instance, that the blood contains an anti-thyroidal substance, and this has been isolated as an independent substance from the protein of the blood, with which it forms a loose combination. A prolonged treatment of rabbits with injections of thyroxine leads to a resistance of these animals against thyroxine, and to the appearance of serologic antibodies detectable by the complement fixation reaction. Preparations containing the thyroidal antihormone have been employed in the treatment of exophthalmic goitre, but their use has not met with any large measure of success. (*See also under ANTERIOR PITUITARY.*)

Serologic antibodies may also be detected, following prolonged treatment with thyroxine, diiodotyrosine, epinephrine, and frequently insulin and phenol. Most patients with hyperthyroidism give the same positive serum reaction, whereas in other individuals the reaction is negative as a rule. The complement fixation reaction is to be obtained in almost the same way with different antigens: thyroxine, diiodotyrosine, epinephrine, sympatol, insulin, tyrosine and phenol. Three patients with spontaneous hypoglycæmia gave a positive reaction, one of



them with only insulin as antigen. It is apparent that different degrees of endocrine hyperactivities, such as hyperthyroidism and hyperinsulinism, as well as experimentally produced states of hyperhormonisation in animals, may give rise to the appearance of non-specific serologic antibodies.—J. Bauer, *J. Amer. med. Ass.*, ii/1937, 1442.

**HYPERTHYROIDISM.** A new treatment has been suggested by Clutton, Harrington and Yuill, who attached thyroxine chemically to proteins and used these to form antigens. The antibodies these substances produced in rabbit's blood were found to neutralise the effects of both thyroglobuline and thyroxine when injected into rats. This work has a wider significance, in that it may be applied to prepare specific antidotes to all sorts of drugs.—J. H. Gaddum, *Pharm. J.*, i/1939, 27.

An extract of an antithyrotropic substance prepared from horse serum after injection of thyrotropic hormone. The substance obtained does not antagonise action of thyroxine but *does* depress the metabolic rate of normal animals and inhibits the action of the thyrotropic hormone in normal and hypophysectomised rats.—E. M. Anderson and J. B. Collip, *Lancet*, i/1934, 784.

**Antithyroidin "Mœbius"** (Merck, Darmstadt; Martindale, London). Thyroidectomised sheep's serum. In exophthalmic goitre. By intramuscular injection or in the form of fluid serum or tablets.

**Thyroidectin** (Parke, Davis, London). A powder prepared from the dried blood of thyroidectomised animals, available in capsules. *Dose*.—1 or 2 capsules thrice daily. In Graves' disease.

### Parathyroideum (B.P.C.).

*Dose*.— $\frac{1}{20}$  to  $\frac{1}{10}$  grain (0.003 to 0.006 g.).

The external parathyroid glands of the ox—dried and powdered. Should be free, or almost free, from thyroid and thymus. It does not contain iodine.

The fresh parathyroid glands weigh on an average 0.09 g. and yield from 0.015 to 0.02 g. of desiccated powder, *i.e.*, 1 = 5 of fresh substance.

The parathyroids are small glands which usually occur in close anatomical relationship to the thyroid gland. They are classified into external and internal—terms which relate to embryological development and do not necessarily denote their position in relation to the thyroid gland, although the external glands are usually found outside the capsule of the thyroid. In man the parathyroids are four in number—two in each lobe of the thyroid. The two internal parathyroids may be placed within the capsule of the thyroid in man and in the bovine species. In dogs both internal and external parathyroids are centrally placed within the thyroid. Accessory parathyroids are not uncommon and may occur in various situations in the neck and thorax—not infrequently in the thymus gland.

**Physiology.** The parathyroids control calcium and phosphorus metabolism; apart from its importance in the formation of bones and teeth the amount of ionised calcium in the blood serum controls the varying irritability of nerves and the contractility of both voluntary and involuntary muscles, and hence it also influences vascular tone. The normal value for the blood-serum calcium is from 9 to 11 mg. of Ca per 100 ml. of blood. The inorganic phosphorus does not normally exceed 5 or 6 mg. per 100 ml. Removal of the parathyroids is followed by tetany and death in a few days, the serum calcium is reduced, there is increased excretion of calcium and nitrogen, increase in the absolute and relative ammonia in the urine, and increase in the ammonia content of the blood. Hyperparathyroidism is characterised by increased viscosity of the blood, and a depletion of calcium from the osseous system. In hypoparathyroidism there is lowered calcium content of the blood and hyperexcitability of nerves and muscles. The occurrence of methylguanidine in the blood after parathyroidectomy may result

from the action of phosphoric acid on creatinine and it is possible that in hypoparathyroidism methylguanidine may accumulate in the blood in sufficient amounts to be toxic. A detoxicating action has been stated to be a function of the parathyroid glands, but there is insufficient evidence to confirm or disprove this.

The occurrence of two types of cells in parathyroid tissue has been held to denote that the glands may exert two different functions but it is not yet known which cells produce the hormone which controls parathyroid metabolism and what the other function, if any, may be.

**Uses.** Desiccated parathyroid gland has been given orally in tetany, tetany of pregnancy, tetany of childhood, epilepsy, paralysis agitans, sprue (with calcium lactate) and eclampsia. It is generally held that no increase of blood-serum calcium can be detected after oral administration, and *Extractum Parathyroidei* (q.v.) hypodermically is to be preferred.

**Tabellæ Parathyroidei** (B.P.C.). Contain  $\frac{1}{10}$  gr. (0.006 g.).

[P1-87] **Thyrocalc** (*Sharp & Dohme, London*). Tablets containing desiccated thyroid  $\frac{1}{4}$  gr., desiccated parathyroid  $\frac{1}{10}$  gr., calcium lactate 5 gr. For use in calcium deficiencies.

### **Extractum Parathyroidei** (B.P.C.).

**Dose.**—20 to 40 units intramuscularly, a unit being one-hundredth of the amount required to raise the blood-calcium of a 20 kg. dog by 5 mg. per 100 ml.

Prepared by extracting parathyroid glands with 5% hydrochloric acid at 100°; after cooling, fat is removed and sodium hydroxide added to pH 8, hydrochloric acid is added to precipitate protein (maximum precipitation occurs at about pH 5.5). The precipitate is removed, redissolved in NaOH and proteins again precipitated by hydrochloric acid. After this process has been repeated several times the filtrates are mixed and contain the active principle of the glands.

For details of method of preparation, see J. B. Collip, *J. biol. Chem.*, 1925, 63, 395; *J. Amer. med. Ass.*, 1/1927, 565. Also J. B. Collip and E. P. Clark, *J. biol. Chem.*, 1925, 63, 133, and 1925, 63, 439.

For methods of biological assay, see Vol. II.

**Liquor Parathyroidei** (U.S.P. XI). **Average dose.**—25 units, by hypodermic injection. One millilitre contains 80 to 120 parathyroid units, each unit being one-hundredth of the quantity required to raise the calcium level of 100 ml. of dog's blood serum by 0.001 g. within 16 to 18 hours after administration.

**Uses.** The chief indication for the use of parathyroid extract is tetany, especially post-operative tetany; it is of less value in infantile tetany and gastric tetany, and is ineffective in other spasmodic conditions such as chorea. It is also stated to be of value in the treatment of lead poisoning, causing the lead to be excreted.

The effects produced by injection of a solution of the parathyroid hormone are (a) increase in the amount of calcium and decrease of phosphorus in the blood; (b) increase in the Ca and P excretion in urine. The calcium is obtained chiefly from the bones. Overdosage may cause kidney damage, rise in blood pressure and accumulation of nitrogenous waste products in the tissues; deposits of calcium may occur in the soft tissues and calculi form in the kidney.

The extract must only be used in conjunction with repeated blood calcium estimations to control its effects. It is safe to give it when the blood calcium is below 9 mg. per 100 ml., but once the level has reached 12 to 13 mg. further administration is both undesirable and unnecessary. The treatment should be immediately discontinued when warning symptoms of overdosage appear, namely, vomiting and diarrhoea.

The rise in blood calcium following injection of the hormone occurs after a latent period of a few hours and persists for about 20 hours. After a few months' treatment, tolerance seems to be established and the effect diminishes.

It is doubtful if parathyroid hormone increases the amount of calcium salts absorbed from the intestine, and in this respect its action differs from that of vitamin D, which increases the serum calcium by increasing absorption from the intestine and the effect may last as long as two weeks after administration has ceased.

In normal subjects parathyroid extract lowers the glycæmia during fasting and increases carbohydrate tolerance, its action being very similar to that of insulin. In ten cases of diabetes intramuscular injection of one millilitre of the extract produced a clear hypoglycæmic effect, slightly lower than that produced by insulin. Administered along with insulin it may increase the hypoglycæmic action of the insulin, or it may scarcely modify it or even slightly inhibit it; given alone parathyroid extract has an undoubted insulin-like action.—A. Ferrannini, *Políclinico*, 1935, 366.

In persons suffering from acute nephritis, parathormone produces a much smaller phosphate diuresis than when they have recovered. The hypothesis that parathormone acts directly on the kidneys to produce an increase of phosphate excretion is thus confirmed.—H. K. Goadby, *Biochem. J.*, 1937, 1530.

**HYPOPARATHYROIDISM.** Although substitution therapy, consisting of the subcutaneous or intramuscular injection of parathyroid extract, is the most specified treatment for chronic post-operative hypoparathyroidism, there are serious objections to the long continued use of this extract, and if successful management can be accomplished without it it is advisable not to use it, since its effectiveness is completely lost in many persons after a period of continuous use. These patients can be maintained in a state of good health by feeding a low phosphorus diet and large amounts of calcium salt—preferably a solution of calcium lactate in amounts sufficient to provide from 1.5 to 2.5 g. of calcium daily. Vitamin D in large amounts is of definite value.—R. H. Freyberg *et al.*, *J. Amer. med. Ass.*, ii/1936, 1774.

**OSTEITIS DEFORMANS** in a woman aged 54 much improved by 5 to 10 units of Parathormone daily for two years with periods of intermission. The serum calcium was normal and 30 gr. of sodium acid phosphate were given daily to decrease absorption of calcium and increase excretion in urine.—G. H. Colt and A. Lyall, *Brit. med. J.*, ii/1933, 10.

**TETANY.** The treatment of infantile tetany by Parathormone is a profound mistake. Although Parathormone bears a superficial resemblance to vitamin D in its effect in raising the blood calcium, Parathormone, so far from having a vitamin D-like effect does not influence calcium or phosphate absorption in rickety conditions, but has, in fact, a definitely deleterious action, aggravating the underlying error, draining still further minerals from the impoverished bones and causing a net loss to the body as a whole. Vitamin D is the proper remedy for infantile tetany.—L. J. Harris, *Brit. med. J.*, ii/1933, 372.

While Collip's Parathormone is active in raising the level of the serum calcium and relieving the symptoms of parathyroid tetany it is not satisfactory unless injected in large and repeated doses. It is also expensive. In most cases, therefore, it is impracticable to employ it. Calcium chloride (*q.v.*) intravenously or *per os* is an excellent emergency measure.—D. Campbell, *Lancet*, i/1935, 369.

The fact should be emphasised that the phosphorus content of the diet must be maintained at a relatively low level during administration of parathyroid before the conclusion is reached that this latter agent is ineffective. If this is done there will be fewer instances of refractoriness to solution of parathyroid in parathyro-privic tetany.—A. Cantarow, *J. Amer. med. Ass.*, i/1939, 1748.

**RADIUM POISONING.** Parathyroid extract and a low calcium diet slightly increased radium elimination in three cases.—Craven and Schleendt, *J. Amer. med. Ass.*, i/1935, 959.

**Euparotone** (Allen & Hanburys, London). Biologically standardised solution of parathyroid hormone, 20 units per ml. *Dose.*—In adult tetany, 20 to 60 units daily in 8-hourly doses may be necessary; in infantile tetany, 10 to 20 units daily may suffice. In other conditions, 10 to 20 units daily or every second day.

**G.R.H. 141** (Allen & Hanburys, London). An extract of parathyroid free from the serum-calcium regulating factor (Collip) and containing a growth-retarding principle. *Dose.*—2 ml. daily subcutaneously. Effective in controlling abnormal cell-growth in a number of conditions.

**Parathormone** (Lilly, London). A solution of the active principles of the parathyroid glands. Is standardised on the relationship between the dose given and the increase in blood-serum calcium, the unit of potency being 0.01 of the amount of extract that produces an average rise of 5 mg. in blood-serum calcium in a 20-kilo dog in 15 hours. *Dose.*—Varies with individuals and conditions. Infantile tetany may be relieved by 10 to 20 units a day, but repeated serum determinations should be made to estimate the reactions. In tetany daily doses of 20 to 60 units are used. It is usually given subcutaneously though it may also be given intramuscularly or intravenously. Calcium gluconate or calcium lactate in large doses *per os* should accompany its use. Excessive dosage leads to increased concentration of calcium and phosphate in the blood, and their increased excretion.

**Paroidin** (Parke, Davis, London). Parathyroid extract standardised on its ability to raise the blood-serum calcium of normal dogs. It is supplied in solution containing 100 units per ml., the unit being one-hundredth of the amount necessary to raise the blood-serum calcium by 1 mg. per 100 ml. *Dose.*—20 to 40 units subcutaneously or intramuscularly.

## TRAGACANTHA

*B.P., U.S.P. XI, P. Helv. V, Fr. Cx., etc.*

From *Astragalus gummifer* and some other species (Leguminosæ). Known in commerce as Persian Tragacanth.

It occurs in thin ribbon-like flakes, known as "flake" tragacanth, and in tears or more rounded masses called "Vermicelli" tragacanth. The power of forming mucilages varies greatly in the different grades.

Hog gum from species of *Prunus*, and Indian tragacanth (*sterculia* or Karaya gum) are used in industry as substitutes.

**Uses.** Widely used as a thickening or suspending agent in the manufacture of creams, jellies and pastes. The mucilage answers well for suspending Tinct. Jalapæ, Liquor Quininae Ammoniatæ, Tinct. Cannabis and Tinct. Myrrhæ, but is useless for Tinct. Benzoini Co. and Tinct. Tolu. For these a mixture of mucilage of tragacanth and mucilage of acacia is best. In the case of a mixture containing 1 dr. of resinous tincture to the ounce, dilute 1 dr. of mucilage of acacia with as much water as possible, add the tincture, and lastly add the mucilage of tragacanth. For other resinous tinctures mucilage of acacia alone yields satisfactory mixtures. The mucilage is best diluted with as much water as possible, and

the tincture then added. Tinctura Hydrastis should have an addition of mucilage of tragacanth if salts are present. Tinctura Lupuli and Tinctura Cimicifugæ require no addition either in presence or absence of salts. Tinctura Podophylli requires no suspending agent in the absence of salts, but if any are present mucilage of acacia is best.

**Cremor Emolliens (U.C.H.).** *Syn.* SKIN CREAM.

Tragacanth 1, methylated spirit 7, glycerin 14, olive oil 3½, simple tincture of benzoin 2, water to 100.

**Gelanthum (P.E.H.C.).** Tragacanth 110 gr., acacia 30 gr., gelatin 120 gr., water 10 oz.; mix, heat, filter and add glycerin 6 dr., thymol ½ gr., water to 12 fl. oz. A basis for various applications for skin medication.

**Glycerinum Tragacanthæ (B.P.C.).** 1 in 5½. A pill excipient; must be used sparingly.

**Lotio Tragacanthæ (B.P.C.).** *Syn.* LOTIO EMOLLIENS.

Tragacanth 0.5% w/v with spirit of chloroform, tincture of tolu, Cologne spirit, glycerin and water.

**Mucilago Tragacanthæ (B.P.).**

*Dose.*—1 drachm to 1 ounce (4 to 30 ml.) or more.

Tragacanth 1½% w/v with alcohol 2½% v/v in chloroform water.

Mucilage made from whole gum has a much higher viscosity than that made from powdered gum and, if not heated, increases in viscosity on keeping. There is no advantage in adopting any particular method of preparation when the mucilage is to be diluted and used for its power of suspending an insoluble powder.—H. Brindle and H. Burlinson, *Quart. J. Pharm.*, 1934, 492. See also G. Middleton, *ibid.*, 1936, 493, 506.

**Mucilago Tragacanthæ (U.S.P. XI).**

Tragacanth 6% w/w and glycerin 18% w/w, in water. *Fr. Cx.* has 10% w/w, in water.

**Pasta Tragacanthæ Composita (B.P.C.).** *Syn.* PASTA LUBRICANS, CATHETER LUBRICANT.

Tragacanth 1% w/v with boric acid, glycerin, oil of lavender and decoction of chondrus.

[P1] **Catheter Lubricant (Meltzer's Formula).** Triturate tragacanth 3 with glycerin 20, add water 100, sterilise, and add mercury oxycyanide 0.25.

**Pulvis Tragacanthæ Compositus (B.P.).**

*Dose.*—10 to 60 grains (0.6 to 4 g.).

Tragacanth 15%, with acacia, starch, and sucrose. Is used as a suspending agent, 10 gr. to 1 oz. Specially useful for bismuth oxynitrate.

The presence of acacia in compound tragacanth powder results in a considerable reduction in the viscosity and suspending power of the tragacanth constituent and it is suggested that it be omitted.—J. M. Rowson, *Quart. J. Pharm.*, 1937, 404.

**Ceratonie Gummi.** *Syn. and Prop. Name.* CAROB GUM, LUCTIN (*Anglo-Gummiferous Products, London*).

The separated endosperms of the seeds of the locust bean tree, *Ceratonia siliqua*. A substitute for tragacanth.

**Mucilago Ceratonie.** Carob gum 1 g., glycerin 3 ml., benzoic acid 0.15 g., triturate and add water to 80 ml.; heat the mixture on a water-bath for 30 minutes.

Various other formulæ given for carob gum preparations.—W. A. Knight and M. W. Dowsett, *Pharm. J.*, i/1936, 35. The mucilage may be prepared without the use of glycerin.

## TRINITROPHENOL

B.P., U.S.P. XI, P. Jap., Fr. Cx., P. Ital. V, F.E. VIII,  
P. Helv. V.



Syn. ACIDUM PICRICUM, PICRIC ACID, CARBAZOTIC ACID.

[P] "*Picric acid.*"

[S3] "*Picric acid—in substances containing less than 5% of picric acid.*"

Dose.—1 to 5 grains (0.06 to 0.3 g.).

Made from phenol by nitration. It is in yellow, shining, bitter-tasting crystals, which melt at 121° to 123°. Trinitrophenol burns readily and explodes when heated rapidly or when subjected to percussion. For safety in handling it is usually supplied mixed with water, and except in small quantities its sale and storage are subject to legal restrictions. It forms salts with metals, some of which are very explosive.

**Soluble** 1 in 90 of water with yellow colour, 1 in 10 of alcohol 90%, 1 in 50 of chloroform, 1 in 8 of benzene, and about 1 in 20 of ether.

**Antidotes.** Empty stomach by stomach tube, washing out thoroughly with plenty of water. Give raw white of egg and milk freely. Purgative dose of sodium sulphate. Saline infusion.

**Uses.** Picric acid was at one time employed in malaria and as an antipyretic, but it is now seldom used internally, owing to its irritant action on the stomach and kidneys. After absorption it stains the skin and mucous membranes a yellow colour; the urine also is coloured yellow or red.

Externally, it is a powerful antiseptic and a 1% aqueous or alcoholic solution may be employed for pre-operative skin sterilisation. The 1% aqueous solution has been widely used in the treatment of burns, sterile gauze being soaked in the solution and placed over the burnt area. It should only be employed, however, in trivial burns, since poisoning may result from absorption if it is employed over a large area. The lotion has been used in addition in the treatment of eczema, erysipelas and other inflammatory skin conditions, but the staining of the skin and the fact that it may give rise to a rash militate against its usefulness. In stomatitis mercurialis a watery paste has been applied every two days and is stated to relieve the pain and remove the ulceration.

**BURNS.** W. M. Dennison states that from 1932 to 1934 he saw so many examples (at the Royal Hospital for Sick Children, Glasgow) of the toxic erythematous rash which can be produced by picric acid that he hesitates to use it even as a first-aid treatment in children.—*Lancet*, ii/1939, 1107.

**ERYSIPELAS.** Daily painting of the affected area and of the skin for a short distance round it with a 3% alcoholic solution of picric acid, then applying lint wrung out of lead lotion, re-applied, when it dries, causes the disease to undergo rapid resolution.—J. G. Watkins, *Practitioner*, ii/1933, 112.

**HYDROCELE.** After having tapped the hydrocele 50 to 70 ml. of a saturated aqueous solution of picric acid at about 100°F. is injected in the direction of the parietal layer of the tunica vaginalis. The solution is prepared by dissolving 1½

drachms of picric acid in 5 ounces of warm distilled water. The scrotum is gently massaged for 5 to 10 minutes and the solution withdrawn. The procedure is then repeated. The next day the patient is allowed to follow his occupation. The method is practically painless and the immediate and remote results excellent. In order to avoid shock, special care should be taken to inject the warm solution slowly and to keep the patient in a recumbent position.—J. Di Pace, *per Practitioner*, ii/1939, 123.

**Carbasus Trinitrophenolis** (B.P.C.). *Syn.* PICRIC GAUZE. 2%. Wool impregnated with trinitrophenol is also prepared.

[P1] **Liquor Trinitrophenolis** (B.P.C.). *Syn.* LIQUOR ACIDI PICRICI. 5% w/v in alcohol.

**Lotio Trinitrophenolis** (B.P.C.). *Syn.* LOTIO ACIDI PICRICI. 1% in water. May be diluted with 1 or more parts of water, as required.

A first-aid application for burns; applied on lint or gauze. After 48 hours remove and wash with potassium permanganate 5 gr. in water 16 oz.

Washing with weak ammonia and then with hydrogen peroxide removes the stains.

**Pigmentum Trinitrophenolis et Camphoræ.** *Syn.* PIGMENTUM ACIDI PICRICI ET CAMPHORÆ. Trinitrophenol 2, camphor 50, and alcohol 90% to 100. Ringworm has been treated by painting this over the scalp twice daily, the hair being clipped close and the scalp washed once or twice a week and covered by a calico cap. Generally the ringworm hairs are loosened, and come away with their bulbous portions in from 10 to 30 days. The paint is inflammable.

**Unguentum Trinitrophenolis** (B.P.C.). *Syn.* UNGUENTUM ACIDI PICRICI. 2%. For pruritus of scrotum. Also for burns; it relieves pain, and may be left 48 hours without changing. For burns of the eye it is preferred by some to solution, using a little cocaine solution beforehand.

[P1-81-84] **Dinitrophenol.** *Syn.* 2 : 4-DINITROPHENOL.  
 $C_6H_3(NO_2)_2OH = 184.0$ .

[P1], [81] and [84] "*Dinitrocresols; dinitronaphthols; dinitrophenols; dinitrothymols.*"

[83] "*Dinitrocresols; dinitrophenols—in substances not being preparations for the treatment of human ailments.*"

Yellow crystals sparingly soluble in cold water, readily soluble in hot water and in ether, benzene or chloroform. Given internally it raises the metabolic rate, and has been given in doses of about 5 gr. per day, for the reduction of obesity. Numerous cases of poisoning have occurred, agranulocytosis, cataract and other lesions being produced, and its use is now regarded as inadvisable.

**Antidotes.** Empty stomach by stomach tube, using 2 gallons of 5% sodium bicarbonate solution, or 1 in 2000 potassium permanganate. Oxygen inhalations. Place patient in an ice pack to bring down temperature. Dextrose or dextrose in saline intravenously. Ascorbic acid is said to bring about improvement of the cataract.

Treatment of acute dinitrophenol poisoning.—Tainter, *J. Amer. med. Ass.*, i/1935, 1071.

For numerous references to toxic effects see Vol. I, 21st Edn., p. 753.

[P1-81-84] **Dekrysil** (Crookes Laboratories, London). Capsules containing 0.05 g. of 4 : 6-dinitro-*o*-cresol. *Dose.*—0.0005 to 0.001 g. per kg. body weight. Given as a metabolic accelerator for the treatment of obesity.

Inquest on a young dancer who sought to reduce her weight by treatment which included Dekrysil. Death was found due to nitrophenol poisoning, traces of nitrophenol being found in the intestines and stomach. She had possibly taken 17 capsules in 3 days.—*Lancet*, i/1934, 652.

Dinitro-*o*-cresol is in the region of 5 times as potent as the dinitrophenol compound.—E. C. Dodds and J. D. Robertson, *Lancet*, ii/1933, 1139.

## UREA

*B.P.C.*

$\text{CO}(\text{NH}_2)_2 = 60.05.$

*Syn.* CARBAMIDE.

*Dose.*—15 to 240 grains (1 to 16 g.) thrice daily. May be given in a mixture flavoured with syrup of lemon or orange. Larger doses are frequently given.

Colourless crystals with cooling, saline taste. M.p.  $130^\circ$  to  $132^\circ$ .

*Soluble* 1 in 1 of water, 1 in 5 of alcohol 90%; 1 in 1 of boiling alcohol 90%; insoluble in ether and in chloroform.

*Uses.* Urea is a powerful diuretic and may be employed in a dose of 15 to 30 g. daily with beneficial effect in chronic parenchymatous nephritis (but not in acute nephritis). The ability to excrete urea is markedly impaired when renal damage has occurred and urea is therefore widely employed as a test of renal efficiency (*for details of Urea Concentration Test, see Vol. II*).

The application of a saturated aqueous solution or of urea crystals to infected wounds hastens healing and removes the offensive odour.

When the blood urea is normal, urea is probably the best saline diuretic for general use (240 gr. in 5 ounces of water, flavoured with tincture of orange). It is rapidly absorbed and is almost non-toxic. It is, however, very diffusible and soon reaches about as high a concentration in the oedema fluid as in the blood, so that its power of drawing water from the tissues is probably limited.—T. H. Crozier, *Fractitioner*, i/1940, 516.

Urea is an extremely valuable diuretic and deserves wider popularity than it seems to enjoy at present. All available clinical reports emphasise its complete freedom from untoward actions and its extraordinary constancy of diuretic effect.

While it is usually less dramatic in its immediate effects than the mercurials, it has obvious advantages and may be used to supplement the latter. There are few patients who cannot take it for at least several weeks at a time, and many continue it for months or years without interruption. Syrup of acacia has been specially recommended as a vehicle for urea, its colloidal nature serving to mask the urea quite satisfactorily. After urea has been taken for a few days the blood nitrogen should be determined to ascertain whether it is being properly excreted.—H. M. Marvin, *J. Amer. med. Ass.*, i/1940, 757.

**CARDIAC DROPSY.** Urea in single daily doses of 20 to 40 g. is recommended for combined use with mercurial injections to prolong the periods between injections in case of cardiac dropsy.—M. Winternitz, *Lancet*, i/1940, 879.

**OTITIS MEDIA.** 20 cases of purulent otitis media were treated by drops of a saturated solution of urea 4-hourly, after washing out the meatus with normal saline. The discharge lost its foul odour in a few hours. Some cases cleared up in 36 hours, but the usual time taken was 3 to 6 days.—J. Foulger and L. Foshay, *J. Lab. clin. Med.*, 1935, 1113.

**WOUNDS.** The application of gross quantities of urea crystals or of strong to saturated aqueous solutions to infected wounds of various types definitely hastens healing, and is frequently efficacious when other therapeutic agents are ineffective. It does not irritate the surrounding normal tissue and practically obliterates



all odour from the wound.—H. G. Holder and E. M. MacKay, *J. Amer. med. Ass.*, i/1937, 1167.

The results of urea treatment on a series of 170 cases of infected wounds were so encouraging that the adoption of this method of treatment as a routine in the casualty department of the Royal Free Hospital is under consideration. The wound is syringed free from pus and necrotic material with a saturated solution of urea, excessive moisture removed, and urea crystals liberally applied. Waxed paper is placed next to the crystals to keep them in contact with the wound and to prevent the dressings becoming soaked. Zinc cream is spread over the adjacent skin. There are no contraindications to its use, though pain is sometimes experienced on application.—L. F. Muldavin and J. M. Holtzmann, *Lancet*, i/1938, 549.

Uniformly gratifying results from the use of a 25 to 30% solution in infected wounds and for the irrigation of wound sinuses. The odour from draining wounds is reduced to a minimum.—G. E. Baker, per *J. Amer. med. Ass.*, i/1938, 1874.

**Hausstus Ureæ (C.X.H.).** Urea 15 g., syrup of orange 15 ml., water to 100 ml.

**Hausstus Ureæ Composita (K.C.H.).** Urea 4½ dr., tincture of orange 15 m., water to 3½ oz. Both the above are given for the urea concentration test.

**Urethanium (B.P.C., P. Helv. V).** *Syn.* ETHYL CARBAMATE (*Fr. Cx., P. Dan., F.E. VIII, P. Ital. V*).  
 $\text{CO}(\text{NH}_2)\text{OC}_2\text{H}_5 = 89.06$ .

*Dose.*—¼ to ½ drachm (1 to 2 g.).

Colourless, odourless crystals with saline taste. M.p. 47.5° to 50°, b.p. about 180°.

**Soluble** 1 in 2 of water, 1 in 1 of alcohol 90%, and in ether, chloroform, glycerin and fixed oils.

**Incompatible** with caustic alkalis and with acids.

**Uses.** Mild hypnotic with very low toxicity and marked diuretic effect. Produces normal sleep without after-effects or depressant action on the heart, and is especially suitable for children, the aged, and those with heart affections. In 1 to 2 g. doses it is stated to give relief in severe bronchial asthma. In solution with quinine it is employed in the injection treatment of varicose veins (*for further details, see p. 881*).

**ASTHMA.** Of 30 patients suffering from severe bronchial asthma 14 received considerable symptomatic relief from the use of urethane 1 to 2 g., dissolved in water before administration. Not more than 4 g. daily was given, and it was not used longer than 4 or 5 days in succession. No untoward effects or narcotic action were observed. It is advisable to give urethane before full development of an attack; and in some instances to use 1 g. three times daily over a period of 3 to 4 days.—L. Farmer, *J. Lab. clin. med.*, Feb. 1939, 453.

**Bromoisovalerianylurea (P.G. VI, P. Ned. V, P. Svec. X, P. Dan.).**  $(\text{CH}_3)_2\text{CH}\cdot\text{CHBr}\cdot\text{CONH}\cdot\text{CONH}_2 = 223.0$ . *Syn. and Prop. Names.* BROMISOVALUM (*P. Helv. V*), BROMISOVALERILUREA (*F.E. VIII*),  $\alpha$ -MONOBROMOISOVALERYLUREA, BROMVALERYLUREA (*P. Jap. V*), BROMURAL (*Knoll, London; Savory & Moore, London*), DORMIGENE (*Allen & Hanburys, London*).

*Dose.*—5 to 10 grains (0.3 to 0.6 g.). *P. Helv. V* has max. single dose 15 grains, max. in 24 hours 30 grains approx.

White, crystalline powder with slightly bitter taste. M.p. 145° to 150°.

**Soluble** 1 in about 450 of water; readily soluble in alcohol and ether.

**Uses.** Hypnotic, inducing sleep in from 5 to 25 minutes after ingestion. The effect lasts from 4 to 5 hours, and may be followed by natural sleep. It is claimed to be useful as a nerve sedative and for inducing sleep in functional nervous disease. It is of no value in insomnia associated with pain.

**Sonasta** (*Christy, London*). Tablets each containing ethylbromoisovaleryl-carbamide 0.22 g., and oxypropionylaminoethoxybenzene 0.12 g. *Dose*.—As soporific, 2 to 3 tablets one hour before retiring; as sedative, 1 to 2 tablets 3 to 4 times a day.

**Elbon-Ciba** (*Ciba, Horsham*). Cinnamyl-*p*-oxyphenylurea,  $C_6H_5 \cdot NH : CH \cdot CO \cdot OC_6H_4 \cdot NH \cdot CO \cdot NH_2 = 282.1$ , in 0.5 g. tablets.

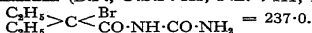
*Dose*.—In tuberculosis: 1 tablet every 3 hours (8 per 24 hours), increased if no response, then decreased. In hay-fever, prophylactically: 1 tablet twice a day, increased during hay-fever season to 2.

Stated to have antipyretic and antiseptic action. Used in pulmonary tuberculosis, for infectious catarrhs of respiratory tract, and in chronic endocarditis; also for hay-fever and asthma.

**Surfen** (*Bayer Products, London*). Bis-2-methyl-4-aminoquinolyl-6-carbamide hydrochloride. A non-staining antiseptic for wounds, etc., used in 0.1 to 0.2% solution. For cystoscopy and irrigation of the bladder, 0.01% solution with 8 drops of dilute acetic acid per 100 ml. (to prevent turbidity in contact with urine).

[P1-S1-S4] **Somnosol** (*Napp, London*).  $\alpha$ -Bromisovalerianylurea 5 gr., amidopyrine  $2\frac{1}{2}$  gr. *Dose*.—Sedative, 1 to 3 tablets thrice daily; soporific, 1 to 3 tablets with a hot drink.

**Carbromalum** (*B.P., U.S.P. XI, F.E. VIII, P. Dan.*).



*Syn. and Prop. Names.* URADAL,  $\alpha$ -BROMO- $\alpha$ -ETHYLBUTYRYL-CARBAMIDE, BROMODIETHYLACETYLUREA, BROMDIETHYLACETYL-CARBAMIDUM (*P. Belg. IV, P. Svec. X*), BROMADALUM (*P. Helv. V*), DIETHYLBROMOACETYLUREUM (*P. Ned. V*), ADALIN (*Bayer Products, London*) (*P.G. VI*), NYCTAL (*Sitsa, Paris; Roberts, London*), PLANADALIN (*Pharmaceutical Specialities (May & Baker) Ltd., London*).

*Dose*.—5 to 15 grains (0.3 to 1 g.). *U.S.P. XI* average dose 8 grains. *P. Helv. V* gives max. single dose 23 grains, max. in 24 hours 45 grains approx. As a hypnotic, should be given half an hour before bedtime and followed by a hot drink.

Tasteless, crystalline powder. M.p.  $116^\circ$  to  $118^\circ$ .

**Soluble** 1 in about 3000 of water, 1 in 18 of alcohol 95%, 1 in 14 of ether, 1 in 3 of chloroform; slightly soluble in light petroleum. It is also soluble in strong mineral acids, from which it is precipitated by addition of water, and in caustic alkali solutions.

**Uses.** A safe hypnotic of medium strength. Does not produce after-effects. Is useful in insomnia due to worry, overwork or excitement, but is less efficient in insomnia due to pain.

[P1-61-87] **Sedormid** (*Roche Products, Welwyn Garden City*). Allylisopropyl-acetylurea in 4-gr. tablets. *Dose*.—As sedative,  $\frac{1}{2}$  to 1 tablet 2 or 3 times a day. As hypnotic, 1 or 2 tablets (or more) 20 minutes before retiring. Its activity is stated to be midway between that of the barbiturates and of the bromides or valerian. It is rapidly eliminated, thus avoiding accumulation. A sedative for nervous insomnia, Graves' disease, disturbances of menstruation and the climacteric, before operation and as an aid to drug-withdrawal treatment.

Thrombocytopenic purpura, following the use of Sedormid. Two cases.—A. M. Hoffman *et al.*, *J. Amer. med. Ass.*, i/1938, 725. A further case.—A. M. Moody, *ibid.*, 726: *ibid.*, ii/1939, 674. Two more cases.—J. Torrens, *Lancet*, i/1938, 749.

Thrombocytopenic purpura, following prolonged medication with Sedormid. Recovery on discontinuance of the drug.—J. Joekes, *Lancet*, ii/1938, 305. See also C. Miller and M. L. Rosenheim, *ibid.*, 402.

### Symmetrical Ureas and Related Compounds.

**Antrypol** (*British Drug Houses, London*). Symmetrical urea of sodium—*m*-aminobenzoyl-*m*-amino-*p*-methylbenzoyl-1-naphthyl-amino-4 : 6 : 8-trisulphonate. Administered intravenously in isotonic saline in the treatment of trypanosomiasis. It is supplied in ampoules containing 1, 2, and 3 g.

**Suramin.** *Prop. Name.* GERMANIN (BAYER "205") (*Bayer Products, London*).

A complex organic urea, probably a derivative of the type:— $[(SO_3H)_2 \cdot OH \cdot C_{10}H_4NH \cdot CO \cdot C_6H_4NH \cdot CO \cdot C_6H_4 \cdot NH]_2CO$ .

*Dose.*—15 grains (1 g.) intravenously in 10 ml. of water.

A white powder soluble in water or in solution of sodium chloride, but insoluble in alcohol.

**Uses.** Suramin is employed in the treatment of trypanosomiasis. It is advisable to start with 0.5 g. intravenously, and if it is well tolerated, to give 1 g. after 24 or 48 hours, this dose being repeated at weekly intervals up to a maximum of 5 g. Some authorities prefer to give this total of 5 g. within one week, contending that a maximum effect is thus produced on the organisms. If given in the early stages of the disease good results are obtained, but in the later stages tryparsamide is more effective. A recent tendency is to combine the two drugs, giving three 1 g. doses of Suramin during the first week, followed by four or five 2 g. doses of tryparsamide. Suramin is a toxic drug and must be used with care. At the end of a 5 g. course there are often signs of renal irritation, and not infrequently a toxic dermatitis appears, but both of these conditions clear up on cessation of treatment. Optic troubles, *e.g.*, amblyopia, have also been observed.

In addition to its curative employment Suramin also has a definite prophylactic value, a dose of 2 g. conferring protection against both *T. gambiense* and *T. rhodesiense* infection for at least three months. (*For further references to the use of Suramin in trypanosomiasis, see Vol. II.*)

In 1935 Jancsó and Jancsó, having reached the conclusion that Germanin acts by interfering with the carbohydrate metabolism of the trypanosomes, decided to examine the action of the hypoglycaemia-producing guanidine derivatives in experimental trypanosomiasis. They found that a number of these derivatives, especially Synthalin (*q.v.*), exerted a definite therapeutic action on mice infected with *T. brucei*. Subsequently, E. M. Lourie and Warrington Yorke found that while Synthalin does not produce any pronounced degree of hypoglycaemia in the normal animal unless given in doses which produce serious damage to the liver, it exercises *in vitro* a powerful trypanocidal action which is of the same order as that of the aromatic trivalent arsenicals.

This discovery that the trypanocidal action of the Synthalin is a direct one, led to the preparation and examination by King at the National Institute for Medical Research of a large number of guanidines, isothioureas, amidines and amines

with alkyl and alkylene chains, and it was found that certain of the diamidines had a powerful trypanocidal action, both *in vivo* and *in vitro*, and that with the most active member of the series, viz., undecane-1 : 11-diamidine, it was possible to produce permanent cures in approximately 100% of mice and rabbits infected with *T. rhodesiense*. Following this, Ewins took up the investigation and prepared a series of aromatic compounds containing the amidine group, some of which showed a remarkable degree of trypanocidal activity, the most active being 4 : 4'-diamidinostilbene, 4 : 4'-diamidinodiphenoxypropane, and 4 : 4'-diamidinodiphenoxypentane; it was found in addition that these compounds had a marked therapeutic action on leishmania infections. The compounds are now being extensively tried in patients suffering from trypanosomiasis and leishmaniasis, and the early clinical reports (some 400 patients have been treated to date) are sufficiently encouraging to justify an optimistic outlook. The compounds have been given both intravenously and intramuscularly. Owing to their greater solubility, 4 : 4'-diamidinodiphenoxypropane and 4 : 4'-diamidinodiphenoxypentane are more suitable for intramuscular injection than the less soluble diamidinostilbene. The usual dose by the intravenous route has been 0.5 to 1 mg. per kg. bodyweight, and by the intramuscular route 1 to 2 mg. per kg. On many occasions the doses have been repeated daily or on alternate days until 10 or 12 injections have been given. No serious accidents have so far been reported though many of the patients receiving the larger doses by the intravenous route have exhibited transient symptoms as flushing of the face, headache, rapid pulse, sweating, etc. No signs of renal irritation have been observed.—Warrington Yorke, *Trans. R. Soc. Trop. med. Hyg.*, 1940, 33, 463.

**Moranyl.** *Syn.* FOURNEAU 309 (*Société Parisienne d'Expansion Chimique, Paris*). The symmetrical urea of disodium *m*-aminobenzoyl-*m*-amino-*p*-methylbenzoyl-1-naphthylamino-4 : 6 : 8-trisulphonate.

Administered in trypanosomiasis as a 10% aqueous solution in doses up to 10 ml. by subcutaneous or intravenous injection.

**S.U.M. 36** (*British Drug Houses, London*). Sterile isotonic solution of the dissymmetrical urea of *m*-benzoyl-*m*-aminobenzoylaminonaphthol-3 : 6-sodium disulphonate. Solutions contain either 0.002 or 0.01 g. per ml.

*Dose.*— $\frac{1}{2}$  to  $\frac{1}{4}$  grain (0.002 to 0.01 g.) intramuscularly every 5th day on two or three occasions.

In the treatment of gonococcal infections, such as urethritis, vulvitis and ophthalmia; also in very acute cases of gonococcal arthritis.

**S.U.P. 36** (*British Drug Houses, London*). The symmetrical urea of *p*-benzoyl-*p*-amino-benzoyl-1-amino-8-naphthol-3 : 6-sodium disulphonate.

*Dose.*— $\frac{1}{2}$  to  $\frac{1}{4}$  grain (0.005 to 0.02 g.) intramuscularly. Ampoules contain 0.01 g. in 1 ml. Also issued in bulk, 0.1 g. in 10 ml.

In the treatment of inflammatory and septic conditions, especially influenza, colds, broncho-pneumonia, acute pleurisy, puerperal pyrexia, vomiting of pregnancy, and the complications of gonorrhoea.

**S.U.M. 468** (*British Drug Houses, London*) is the symmetrical urea of *m*-benzoyl-*m*-amino-toluyyl-1-naphthylamine-4 : 6 : 8-sodium trisulphonate.

*Dose.*—0.001 to 0.002 g. intramuscularly.

In the treatment of thrombosis, pemphigus and other infections caused by micro-organisms of the proteus group.

**S.U.P. 468** (*British Drug Houses, London*) is the symmetrical urea of *p*-benzoyl-*p*-aminobenzoyl-1-aminonaphthalene-4 : 6 : 8-sodium trisulphonate.

*Dose.*—0.001 to 0.003 g. intramuscularly. In the treatment of acute streptococcal infections and in chronic streptococcal arthritis.

## VALERIANA

*B.P., U.S.P. XI, P. Helv. V, Fr. Cx.*

*Dose.*—5 to 15 grains (0.3 to 1 g.). *U.S.P. XI* average dose 12 grains.

The dried rhizome and roots of *Valeriana officinalis* (*Valerianaceae*), collected in the autumn.

As a war emergency measure, when valerian is prescribed or demanded, Indian valerian may be dispensed or prescribed.

The odour may be removed from a scale pan or from the hands by rubbing with sodium bicarbonate.—R. G. Murrison, *Pharm. J.*, i/1935, 106.

**Uses.** Given in hysterical and neurotic conditions as a sedative. Its action has been attributed to its unpleasant smell, and if this is so, deodorised preparations cannot possess any activity due to their valerian content.

**Alcoolature de Valériane Stabilisée** (*Fr. Cx.*). Made by adding the fresh entire roots to an equal weight of 95% alcohol while maintained boiling on the water-bath for 20 minutes, allowing to cool and repeating the process, finally making up any loss.

**Elixir Valerianæ** (*B.P.C.*).

**Dose.**— $\frac{1}{2}$  to 2 drachms (2 to 8 ml.). Simple tincture of valerian, 1 in 3, with extract of liquorice and aromatic elixir.

[P1] **Elixir Valerianæ Compositum** (*B.P.C.*). *Syn.* ELIXIR BROMIDI ET VALERIANÆ COMPOSITUM.

**Dose.**— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.).

Contains potassium bromide  $7\frac{1}{2}$  gr., chloral hydrate  $7\frac{1}{2}$  gr., and liquid extract of valerian 15 m., with oils of orange, lemon, coriander and anise, in alcohol, syrup and water to 1 oz. To avoid waste the quantities of each of the four volatile oils should be reduced by 25%.

**Extractum Valerianæ** (*B.P.C.*).

**Dose.**—1 to 5 grains (0.06 to 0.3 g.).

The evaporated 70% alcohol percolate.

**Extractum Valerianæ Liquidum** (*B.P.C.*).

**Dose.**—5 to 15 minims (0.3 to 1 ml.). 1 in 1, from freshly dried valerian.

**Infusum Valerianæ Concentratum** (*B.P.C.*).

**Dose.**— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.). 1 in 5.

**Infusum Valerianæ Recens** (*B.P.C.*).

**Dose.**— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.). 1 in 40.

**Mist. Pot. Brom. et Valerian.** (*N.I.F.*). Potassium bromide 10 gr., ammonium carbonate  $2\frac{1}{2}$  gr., concentrated infusion of valerian 30 m., water to  $\frac{1}{2}$  oz.

**Mistura Valerianæ Composita** (*B.P.C.*).

**Dose.**— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.).

Potassium bromide 10 gr., ammoniated tincture of valerian 10 m., camphor water to 1 oz.

**Tinctura Valerianæ Ammoniata** (*B.P.*).

**Dose.**— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.). Valerian 1 in 5, with dilute solution of ammonia 1 in 10, oils of lemon and nutmeg and alcohol 60%. An antispasmodic and nervine tonic.

**Tinctura Valerianæ Simplex** (*B.P.C.*). *Syn.* TINCTURA VALERIANÆ.

**Dose.**—1 to 2 drachms (4 to 8 ml.). 1 in 8 in alcohol 60%.

**Valeriana Indica (B.P.C.).**

*Dose.*—5 to 15 grains (0.3 to 1 g.).

Indian valerian consists of the dried rhizome and roots of *V. Wallichii*.

*Uses.* As for valerian. As a war emergency measure (1941), it may be dispensed or supplied when valerian is prescribed or demanded.

[P1] **Elixir Bromo-Valerianate Gabail** (*Anglo-French Drug Co., London*). Stated to contain extract of valerian (deodorised) 4.00 g., valerianic acid (deodorised) 1 g., ammonium carbonate 2.5 g., chloral hydrate 4 g., strontium bromide 4 g., syr. aurant. (*Fr. Cx.*) 100 g., distilled water 100 g.

[P1] **Elixir Valibrom** (*British Drug Houses, London*). Odourless extract of valerian with chloral formamide 10 gr., and potassium bromide 20 gr. per oz.

[P1] **Elixir Valibrom Compound** contains opium alkaloids equivalent to 0.03% of anhydrous morphine.

**Euvalerol** (*Allen & Hanburys, London*). Compound elixirs of valerian. "A": 1 oz. = 1 dr. of ammoniated tincture of valerian. [P1-81-84] "B": Elixir "A" with phenobarbitone  $\frac{1}{2}$  gr. per dr. "C": Elixir "A" with ammonium bromide 30 gr. and strontium bromide 15 gr. per oz. *Dose.*—1 to 2 teaspoonfuls thrice daily in each case.

**Valerianate (Gabail)** (*Anglo-French Drug Co., London*). Non-alcoholic extract of valerian root, deodorised. *Dose.*—1 teaspoonful 3 or 4 times daily.

**Acidum Valerianicum (Fr. Cx., P. Helv. V).**

*Dose.*—1 to 5 minims (0.06 to 0.3 ml.), in syrup or in gelatin capsules.

Consists principally of optically inactive isovalerianic acid,  $(CH_3)_2 \cdot CH \cdot CH_2 \cdot COOH$ , with more or less dextrorotatory methyl-ethylacetic acid,  $(C_2H_5)(CH_3)CH \cdot COOH = 102.1$ .

An oily liquid, sp. gr. about 0.93, soluble 1 in 30 of water, from which it separates on the addition of soluble salts such as calcium chloride. It is miscible with ether and alcohol.

Given in hysteria and nervous affections.

**Ammonii Valerianas (Fr. Cx.). Syn. AMMONII VALERAS.**

*Dose.*—1 to 8 grains (0.06 to 0.5 g.). In masses of flat, colourless, deliquescent crystals, with a strong valerian odour, very soluble in water and alcohol. As supplied commercially it is an acid salt containing ammonia equivalent to only 35% of  $C_4H_9 \cdot COONH_4$ . A 25% aqueous solution is prepared for dispensing.

**Soluté de Valérianate d'Ammoniaque Composé (Fr. Cx.).**

*Dose.*—2 to 4 drachms (7 to 15 ml.).

Valerianic acid 3, ammonium carbonate *q.s.* (about 4) to neutralise, extract of valerian 2, alcohol 90% 5, orange-flower water to 100, all by weight. A "nerve tonic".

**Amyl Valerianate.  $C_5H_{11} \cdot C_4H_9O_2 = 172.2$ .**

The isomyl ester of isovalerianic acid. A mobile liquid, sp. gr. 0.858. Miscible with alcohol. Is known as "Apple Essence."

**Ferri Valerianas. Syn. FERRI VALERAS.  $Fe_2(C_4H_9O_2)_2(OH)_4 = 381.9$ .**

*Dose.*—1 to 5 grains (0.06 to 0.3 g.).

A dark red or brown amorphous powder with slight odour. Insoluble in water, soluble in alcohol 90%. A nerve stimulant and emmenagogue, and has been used in anæmia.

**Sodii Valerianas (B.P.C.). Syn. SODII VALERAS.  $C_4H_9O_2Na = 124.1$ .**

*Dose.*—1 to 5 grains (0.06 to 0.3 g.).

In white hygroscopic masses, soapy to the touch. Used as a nerve sedative in hysteria and other neurotic conditions.

**Zinci Valerianas (B.P.C.). Syn. ZINCI VALERAS.**  
 $(C_4H_9 \cdot COO)_2Zn \cdot 2H_2O = 303.6$ .

White powder or in pearly crystals with valerianic odour and sweet astringent taste.

**Soluble** 1 in 120 of water, 1 in 60 of alcohol 90%, 1 in 500 of ether.

**Incompatible.** Acids and metallic salts. (See also zinc salts.)  
Used similarly to other valerian preparations.

**Neo-Bornyval** (*Riedel-de Haen, Berlin; Endocrines-Spicer, Watford*). *iso*-Valerylglcollic ester of borneol. Perles contain 0.25 g. *Dose*.—1 or 2 perles twice or thrice daily. Cardiac neurosis, nervous gastric troubles, etc.

[D-P1-81] **Trivalin** (*Saccharin Corporation, London*). *Dose*.—Hypodermically, 8 to 15 minims ( $\frac{1}{4}$  to 1 ml.) once to 3 times daily. A solution containing per ml. 0.0037 g. ( $\frac{1}{27}$  gr.) of caffeine valerianate, 0.0054 g. ( $\frac{1}{36}$  gr.) of cocaine valerianate and 0.019 g. ( $\frac{3}{8}$  gr.) of morphine valerianate. Also available in capsules. Said to have the therapeutic effects of morphine without disadvantages. Anodyne, e.g., in painful dressings, inoperable cancer, gallstone colic and neuralgia. Is also made in combination with hyoscine valerianate  $\frac{1}{18}$  grain (0.00056 g.) per ml., for treatment of the insane. *Dose*.—0.25 to 0.5 ml. daily.

**Valisan** (*Schering, London*). Borneol ester of bromoisovalerianic acid. *Dose*.—2 or 3 perles of 3.75 grains several times a day.

**Valyl** (*Bayer Products, London*). Valeryldiethylamide. *Dose*.—2 or 3 perles of 0.125 g. several times a day.

**Castor** (*B.P.C., P. Austr.*).

The dried preputial follicles and secretions from the beaver, *Castor fiber* (Rodentia), in brown pieces. *Fr. Cx.* describes the two commercial varieties, Canadian and Russian. Contains from 35 to 70% of alcohol-soluble matter. Stimulant and antispasmodic. Is given in dysmenorrhœa as tincture.

**Tinctura Castorei** (*B.P.C.*).

*Dose*.— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.). 1 in 20. It must be suspended in water with mucilage of acacia.

**Sumbul** (*B.P.C.*). *Syn.* MUSK ROOT. Dried transversely sliced root of *Ferula Sumbul* (Umbelliferae). Used as nerve sedative and anti-hysterical.

**Tinctura Sumbul** (*B.P.C.*).

*Dose*.— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.). 1 in 10. When diluted it requires addition of mucilage of acacia to suspend the resin.

## ZINCUM

Zn = 65.38.

**Incompatibilities of Zinc Salts.** Alkaline carbonates, and alkalis in general, vegetable infusions and milk.

**Antidotes.** Do not use emetic or stomach tube, patient is probably vomiting. Give copious draughts of sodium or potassium bicarbonate dissolved in warm water. Keep patient lying down; apply heat to abdomen. Give demulcents, such as milk and eggs, freely. Tannic acid or medicinal charcoal has been used. Morphine,  $\frac{1}{4}$  gr. hypodermically, if pain is severe.

**Zinci Acetas** (*B.P.C., U.S.P. XI*).

$\text{Zn}(\text{CH}_3\text{COO})_2 \cdot 2\text{H}_2\text{O} = 219.5$ .

*Dose*.—1 to 2 grains (0.06 to 0.12 g.). 10 grains (0.6 g.), or more, as an emetic.

White crystals with faint acetous odour. Soluble 1 in 2.5 of water, about 1 in 40 of alcohol 90%. Used as astringent lotion ( $\frac{1}{4}$  to 1%).

**Zinci Bromidum (B.P.C.).**  $\text{ZnBr}_2 = 225.2$ .

*Dose.*—2 to 5 grains (0.12 to 0.3 g.) in water.

White deliquescent powder. Soluble 4 in 1 of water, 2 in 1 of alcohol 90% and in ether. A little dilute hydrobromic acid will make a clear solution. Has been used in epilepsy.

**Zinci Carbonas (B.P.C.).** *Syn.* ZINC SUBCARBONATE.

A white impalpable powder varying slightly in composition but approximately corresponding to  $\text{ZnCO}_3, 2\text{ZnO}, 3\text{H}_2\text{O}$ . Insoluble in water and alcohol. Mildly astringent and protective, and occasionally used similarly to the oxide in lotions or dusting powders.

**Zinci Chloridum (B.P., U.S.P. XI, P. Helv. V, Fr. Cx.).**  
 $\text{ZnCl}_2 = 136.3$ .

In deliquescent sticks, masses or granular powder. Owing to presence of oxychloride it is not completely soluble in water, but solutions clear on neutralising to methyl orange with hydrochloric acid.

**Soluble** 1 in less than 1 of water, 1 in about  $1\frac{1}{2}$  of alcohol 90%, 1 in 2 of glycerin, and in ether.

**Uses.** A powerful, odourless caustic, astringent, antiseptic and anti-putrescent. As a lotion for wounds and ulcers 10 to 20 gr. per oz. is used. A paste prepared with starch and glycerin is sometimes used in lupus and for ulcers. As an astringent antiseptic in ophthalmology, solutions containing  $\frac{1}{2}$  to 2 gr. per oz. are used.

In the treatment of erosion of teeth, is useful to touch painful spots, or the addition of a little to chloroform-mastic forms a useful paint. (The zinc chloride must be dissolved in a small quantity of dehydrated alcohol, with a trace of hydrochloric acid if necessary, and added to the chloroform-mastic solution.)

**TUBERCULOUS ULCERATION.** Pain abolished and ulcerations healed after 5 applications of solution of 3 g. zinc chloride in 10 ml. of 80% alcohol. Repeat every 3 weeks: tincture of iodine applied daily.—*per J. Amer. med. Ass.*, i/1927, 1039.

**Collutorium Astringens (R.D.H.).**

Zinc chloride 5 gr., zinc sulphate 10 gr., water to 1 oz.

*U.C.H.* uses zinc chloride 0.4, zinc sulphate 0.4, spirit of chloroform 0.4, aniline yellow q.s., dilute hydrochloric acid 0.15, peppermint water to 100. Use half a teaspoonful to half a tumblerful of water.

**Collyrium Zinci Chloridi (B.P.C.).** 0.1% w/v.

**Guttæ Zinci Chloridi (R.L.O.H., St. T.H.).**  $\frac{1}{2}$ , 1 or 2 gr. per oz.

**Guttæ Zinci Chloridi cum Alcohol (Brompton H.).** Zinc chloride 5 gr., alcohol 90%  $\frac{1}{2}$  oz., water  $\frac{1}{2}$  oz. For Eustachian self-inflator.

[D-P1-81] **Guttæ Zinci Chloridi cum Cocainæ Hydrochlorido.**

$\frac{1}{2}$ , 1 or 2 gr. with cocaine hydrochloride 10 gr. per oz.

**Injectio Zinci Chloridi (L.H.).** For vaginal use.

Zinc chloride 5 gr., water to a pint.

**Liquor Zinci Chloridi (B.P.C.).**

Contains the equivalent of about 40% w/v of zinc. Sp. gr. 1.53.

4 m. of this solution = 3 gr. of solid zinc chloride. On diluting, a trace of hydrochloric acid will be necessary to clear it.

**Lotio Zinci Chloridi (R.L.O.H.).**  $\frac{1}{2}$  or 1 grain to 1 ounce.



**Zinci Oxidum** (B.P., U.S.P. XI, P. Helv. V, Fr. Cx.).  
ZnO = 81.38. *Syn.* FLORES ZINCI (P. Jap. V).

*Dose.*—5 to 10 grains (0.3 to 0.6 g.).

Has been used for nervous debility, migraine, hysteria, and for the night-sweats of phthisis. Chiefly employed externally as a mild astringent and protective in ointments, lotions and dusting powders for skin affections.

Has definite bactericidal properties. While it is almost neutral so far as the cells of the skin are concerned, it is split up by acid-producing microbes into disinfectant compounds.—Haxthausen, per *Prescriber*, 1929, 330.

**MUSTARD GAS BURNS.** The following cold cream was found soothing and protective: zinc oxide 360 gr., oil of lavender 30 m., powdered tragacanth 360 gr., hydrous wool fat 240 gr., lime water to 6 ounces.—R. J. Rowlette, *Practitioner*, ii/1940, 202.

**VINCENT'S ANGINA.** The condition may be successfully treated by packing the gum margin with a paste prepared by mixing zinc oxide with eugenol or oil of cloves. Wisps of cotton wool are saturated with the mixture and tucked into the interdental spaces, especially between the loose gum margins and the teeth. It is of first importance that the dressing be carried into the parodontal sulcus all round every tooth, but without pressure and without causing pain. More wisps are spread over the first and pressed into place with a moist swab and smoothed over with a gloved finger. The mixture rapidly sets in the presence of moisture and forms a light cement casing over the gum margins. The results are very satisfactory. Within a few hours all pain and distress ceases and the patient can at once resume normal diet. When the dressing is removed 48 hours later, the gum margin is a delicate pink colour, and entirely free from slough, acute inflammation or undue tenderness. It is advisable, however, to repeat the dressing for a further four days. After-care is important and consists in applying daily friction to the epithelium covering the gum margins.—E. W. Fish, *Lancet*, ii/1938, 558.

**Cremor Zinci** (B.P.C.). Zinc oxide 32% in wool fat, almond oil and solution of calcium hydroxide.

**Cremor Zinci** (St. M. H.).

Zinc oxide 480 gr., wool fat 3 dr., olive oil 1 oz., solution of calcium hydroxide 1 oz. Useful in acute eczema in the drying stage where there is much redness.

**Cremor Zinci cum Calamina** (Mid. H.). Zinc oxide 30 gr., calamine 30 gr., thymol 2 gr., hydrous wool fat 2 dr., liquid paraffin to 1 oz. For eczema of the meatus.

**Emplastrum Zinci Oxidi** (B.P.C.). Spread with a rubber adhesive compound containing not less than 20% of zinc oxide.

**Gelatinum Zinci** (B.P.). *Syn.* UNNA'S PASTE.

Zinc oxide 15% in a glycerin-water-gelatin base. For use it is melted and applied with a brush to eczematous surfaces. Ichthammol, resorcinol and other medicaments may be added.

**VARICOSE ULCERS** treated by the above after thoroughly cleansing the leg or foot with soap and spirit, alcohol, mercuric chloride solution 1 in 4000 to 1 in 2000, or 1 in 40 carbolic lotion. The paste, previously melted and cooled, is poured over the ulcer. The part is then dried and the paste is bandaged on with a gauze bandage. Another layer of paste is applied; this is covered with a bandage, and so on until four layers have been applied. May be left in many cases undisturbed for weeks, but it is safer to dress again after 2 or 3 days with salicylic talc if any discharge. It forms a new skin, pliable and slightly elastic.

A preparation of the composition zinc oxide 1, gelatin 2, glycerin 3, water 4 parts, of value in arthritis, dermatitis, erysipelas, erythema nodosum and simplex, myositis, periostitis, phlebitis and varix of the leg, synovitis, "tennis leg," minor thrombosis, and contusions and sprains of joints or limbs. It is the treatment *par excellence* for chronic varix and acute phlebitis. Method of preparation and application of dressings.—W. Muir Smith, *Brit. med. J.* i/1927, 137.

**P2] Gelatin Compound Phenolised.** Gelatin 625 parts, zinc oxide 250, glycerin 1900, water 1900 containing 1.5% of phenol. Heat till liquid and apply with brush, apply spiral bandage, and brush on another layer, repeat to total of three bandages and four layers of the preparation. For chronic ulcers, unhealed secondary burns and varicose veins.—*J. Amer. med. Ass.*, ii/1929, 1809.

A further modified form: Zinc oxide 10, glycerin 10, glue 4, acacia 5, water 30. Spread on bandages for varicose ulcers.—C. J. and K. M. Cellan-Jones, *Brit. med. J.*, ii/1930, 560.

**Gelatinum Zinci et Ichthammolis (B.P.C.).** *Syn.* PASTA ZINCI ET ICHTHAMMOLIS. Ichthammol 2% in a zinc oxide and glyco-gelatin basis.

**Ligamentum Pastæ Zinci (B.P.C.).** *Syn.* ZINC PASTE BANDAGE. Prepared with a paste containing not less than 17% of zinc oxide.

**Pasta Carbonis et Zinci.** Soak gelatin 16 in a portion of the total glycerin required (20), and a portion of the water (50 in all required), for 12 hours. Make a paste of boric acid 6, zinc oxide 6 and charcoal 18 with remainder of liquids, mix on water-bath, and pour into suitable vessel to set.

For leg ulcers the charcoal is a useful addition. Boric lotion fomentation should first be carried out to clean the ulcer. If tending to be sluggish red lotion helps.

**Pasta Zinci cum Amylo (St. M. H.).**

Zinc oxide, starch, liquid paraffin, wool fat, of each equal parts. For intertrigo and excessive perspiration.

**Pasta Zinci Oxidi Composita (B.P.).** *Syn.* ZINC PASTE.

Zinc oxide and starch, of each 25%, in white soft paraffin.

**Pasta Zinci Oxidi cum Acido Salicylico (B.P.C.).** *Syn.* LASSAR'S PASTE.

Salicylic acid 2% in a zinc oxide, starch, and white soft paraffin paste.

Useful in the treatment of skin affections, especially for dry eczema with much scaling. In irritating conditions the acid may be omitted. It may be retained and increased in amount where there is less inflammatory reaction.

**Pasta Zinci Oxidi (Fr. Cx.).** *Syn.* LASSAR'S PASTE (Fr. Cx.). Contains equal parts of starch, zinc oxide, wool fat and Vaseline.

**Pasta Zinci Oxidi cum Aqua (Fr. Cx.).** *Syn.* DARIER'S PASTE. Equal parts of zinc oxide, calcium carbonate, glycerin and water.

**[P1] Pilulæ Zinci Oxidi et Belladonnæ (B.P.C.).**

*Dose.*—1 pill.

Contains zinc oxide 2 gr. and extract of belladonna  $\frac{1}{2}$  gr.

**[P1] Pilula Zinci cum Belladonna (T.H.).**

Zinc oxide 2 gr., extract of belladonna  $\frac{1}{2}$  gr. *Dose.*—1 or 2 at bedtime.

**Pulvis Zinci et Acidi Borici (B.P.C.).**

Equal parts of zinc oxide and boric acid.

**Pulv. Zinc. et Acid. Boric. (N.I.F.).** Boric acid 240 gr., zinc oxide 240 gr., talc 470 gr., salicylic acid 10 gr.

**Pulvis Zinci et Amyli (B.P.C.).**

Equal parts of zinc oxide and starch.

**Pulvis Zinci et Amyli Compositus (B.P.C.).**

Equal parts of zinc oxide, starch, boric acid and purified talc, perfumed with oil of geranium.

**Unguentum Benzoini et Zinci (C.X.H.).** Compound tincture of benzoin 2, ointment of boric acid 4, ointment of zinc oxide 4, olive oil 1. Gives relief in, and stimulates healing of, cracked nipples and small ulcers and fissures.

**Unguentum Wilsoni (P. Jap. V).** *Syn.* WILSON'S OINTMENT.

Zinc oxide 1, benzoinated lard 4.

**Ung. Z.E.B. (N.I.F.).** Ointment of zinc oxide 160 gr., oil of eucalyptus 20 m., yellow ointment of boric acid to 480 gr.

**Unguentum Zinci cum Balsamo Peruviano (B.P.C.).**

Balsam of Peru 4% in ointments of zinc oxide and boric acid.

**Unguentum Zinci cum Benzoino (B.P.C.).**

Compound tincture of benzoin about 1 in 8 in ointment of zinc oxide.

**Unguentum Zinci et Olei Ricini (B.P.C.).**

Zinc oxide and castor oil in benzoinated lard, corresponding to a mixture of equal weights of castor oil and the zinc ointment of the B.P. '14.

**Unguentum Zinci et Olei Ricini cum Benzoino (B.P.C.).**

Zinc oxide, castor oil and compound tincture of benzoin in benzoinated lard.

**Unguentum Zinci Oxidi (B.P.).** *Syn.* UNGUENTUM ZINCI.

Zinc oxide 15% in simple ointment. Does not mix with castor oil (*see* Unguentum Zinci et Olei Ricini).

The zinc ointment of the B.P. is, on the whole, the most generally suitable for all forms of dermatitis.—H. Haldin-Davis, *Brit. med. J.*, i/1935, 289.

**Unguentum Zinci Oxidi (U.S.P. XI).**

Zinc oxide 20, liquid petrolatum 10, wool fat 5, white wax 5, white petrolatum 60.

**Unguentum Zinci Oxidi Compositum (St. T. H.).** *Syn.* IGNOFORM OINTMENT.

Zinc oxide 100 gr., cocoa butter 10 gr., solution of hamamelis 10 m., distilled water 80 m., wool fat 150 gr., yellow soft paraffin to 1 oz.

**Pellanthum (Handford & Dawson, Harrogate).** A water-soluble artificial skin containing 20% of zinc oxide. For skin affections. Is also available with ichthammol and in other combinations.

[P1] **Proctoids (John Wyeth, London).** Suppositories containing zinc oxide 10, boric acid 10, bismuth oxyiodide 1.67, bismuth carbonate 8.33, powdered extract of belladonna 0.5, ephedrine sulphate 0.1, balsam of Peru 1.0, cocoa butter to 100. For hæmorrhoids, pruritus ani, fistula, etc.

**Zinc Oxychloride.** Used as a dental filling. The "powder" is of zinc oxide and the "liquid" zinc chloride solution. Mix thoroughly. Sometimes used as a root-filling and for sensitive dentine; will irritate a live pulp. The following are also used:—

**Zinc Oxyphosphate.** It is supplied in the form of dried powdered zinc oxide in various colours, with the "liquid," which consists of phosphoric acid. These are mixed intimately prior to use as a flooring when not too near the pulp.

**Zinc Oxysulphate.** Consists of calcined zinc sulphate and zinc oxide; mucilage of acacia is used to mass.

**Zinci Sulphas (B.P., U.S.P. XI, P. Helv. V, Fr. Cx.).**

$\text{ZnSO}_4 \cdot 7\text{H}_2\text{O}$  = 287.55.

Dose.—1 to 3 grains (0.06 to 0.2 g.); emetic dose 10 to 30 gr. (0.6 to 2 g.).

**Soluble** 1 in 0.65 of cold water, 5 in 1 of boiling water, 1 in 1 of glycerin; insoluble in alcohol 90%.

**Uses.**  $\frac{1}{4}$  to 1% solutions, frequently combined with alum or sometimes ferrous sulphate, are used for inflammatory conditions

of the mucous membrane, *e.g.*, gleet and gonorrhœa. A 1% solution has been used as an intranasal spray in the prophylaxis of poliomyelitis (*see* Vol. II), but is of doubtful value. 1 in 500 may be added to eye lotions in conjunctivitis. A 0.5% solution requires 1 g. of sodium chloride or 6.5 g. of sodium sulphate per 100 millilitres to render it isotonic with the lachrymal secretion.

Smarting from zinc or copper salts in collyria may be relieved by using a saturated solution of potassium chlorate instead of water.

Experimental evidence indicates that the three types of cells in the sensory epithelium may be destroyed by 1% zinc sulphate and that replacement of only the non-sensory cells occurs. Those who contemplate the use of this solution as a protective (*e.g.*, in poliomyelitis) should be made aware of the destructive effect of this salt on the delicate olfactory mucous membrane.—C. G. Smith, *Canad. med. Ass. J.*, ii/1938, 138.

The loss of the sense of smell, which is an indication of the thoroughness of the treatment and of continued resistance to infection, may become lasting. There are reports of several cases in adults who have not regained their sense of smell after more than six months. Caution about the further use of the spray in man until more is known about the mechanism underlying the protection in monkeys.—E. W. Schultz and L. P. Gebhardt, *J. Amer. med. Ass.*, i/1938, 2024.

**Zinc Sulphate Points** are moulded for intra-uterine use. Points of equal parts zinc sulphate and alum, and of copper sulphate are also made.

**Collyrium Astringens Luteum.** *Syn.* GUTTÆ HORSTI, HORST'S EYE WASH. Ammonium chloride 2, zinc sulphate 5, distilled water 890, dissolve and add camphor 2, dissolved in diluted spirit (sp. gr. 0.895) 100, then add saffron 1. Digest 24 hours and filter. As an astringent lotion it is used for conjunctivitis.

A comprehensive review of the pharmacy of eye lotions covering type of glass for containers, sterilisation and antiseptic agents, isotonicity and pH. Formulæ are given for lotions claimed to be isotonic, sterile, stable and to have the optimum pH, namely 7.8.—F. Henrioul, *J. pharm. Belg.*, 1936 (a series of 15 papers).

**Collyr. Zinci Co. (N.I.F.).** Boric acid 5 gr. and zinc sulphate 1 gr. in water to 1 oz. For use dilute with an equal quantity of hot water.

**Collyrium Zinci Sulphatis (B.P.C.).** 0.2% w/v.

**Guttæ Zinci Sulphatis (R.L.O.H.).**  $\frac{1}{2}$ , 1 or 2 gr. per oz.

**Gutt. Zinc. Sulph. c. Acid. Boric. (N.I.F.).** Zinc sulphate  $\frac{1}{2}$  gr., boric acid 1 gr., distilled water to 2 dr.

**Injectio Zinci Sulphatis (L.H.).** For vaginal use.

Has 60 grains in 1 pint of water, *i.e.*, 0.69% or 1 in 144.9.

**Lotio Potassæ Sulphuratæ (B.P.C.).** *Syn.* LOTIO ZINCI SULPHIDI, LOTIO ALBA.

Contains zinc sulphide freshly precipitated by interaction of 10 gr. of sulphurated potash and 10 gr. of zinc sulphate per oz. of rose water. Acne vulgaris is well treated with this.

**Lotio Rubra (B.P.C.).** Contains zinc sulphate 2 gr., with compound tincture of lavender and water to 1 oz. *R.L.O.H.* is similar but with 1 gr. of zinc sulphate per oz. It is often applied for its astringent effect to ulcers.

[F2] **Lotio Spiritus Sulph. Co. (L.S.H.).** Zinc sulphate 30 gr., sulphurated potash 30 gr., water to 3 oz.; mix and add phenol 1 dr., resorcinol 1 dr., industrial methylated spirit 6 oz.

**Lotio Sulphatum.** Zinc sulphate 30 to 40 gr., alum 30 to 40 gr., ferrous sulphate 20 gr., copper sulphate 2 gr., water to 8 oz.

**Lotio Sulphuris cum Zinco (St.J.H.).** Precipitated sulphur 15 gr., zinc sulphate 15 gr., sulphurated potash 15 gr., water to 1 oz.

**Pessus Zinci Sulphatis (B.P.C.)** contains 5 gr. (0.3 g.).

**Pulvis Zinci Sulphatis Compositus (B.P.C.).** *Syn.* PULVIS ACIDI BORICI COMPOSITUS, PULVIS ANTISEPTICUS SOLUBILIS.

Zinc sulphate, 1 in 8, with eucalyptol, menthol, phenol, thymol, salicylic acid and boric acid.

**Calamina (B.P.C.).** *Syn.* CALAMINA PRÆPARATA.

A basic zinc carbonate, with or without zinc oxide, yielding 68 to 90% of residue (ZnO) on ignition, and suitably coloured with iron oxide. It was formerly obtained by igniting the native carbonate, but is now prepared by precipitation.

**Linimentum Calaminæ (B.P.C.).**

Calamine about 20 gr. and zinc oxide about 15 gr. in an emulsion of liquid paraffin and solution of calcium hydroxide to 1 oz. This preparation has the advantage over similar preparations made with vegetable oils of not becoming thicker on storage.

In chronic eczema, *e.g.*, to a freely-weeping surface with redness and itching, apply with brush or cotton-wool swab, or spread on thin washed butter muslin. Very important that the inflamed surface should not be treated with a hot thick dressing. Perchloride 1 in 3000 to 1 in 2000 may be a desirable addition.

**Linimentum Calaminæ (L.S.H.).** Calamine 40 gr., zinc oxide 20 gr., solution of calcium hydroxide and sesame oil of each  $\frac{1}{2}$  oz.

*St. G.H.*—Calamine 30 gr., zinc oxide 30 gr., glycerin of lead subacetate 6 m., olive oil  $\frac{1}{2}$  oz., solution of calcium hydroxide to 1 oz.

*W.H.*—Calamine 30 gr., zinc oxide 30 gr., wool fat 4 gr., oleic acid 3 m., liquid paraffin  $\frac{1}{2}$  oz., solution of calcium hydroxide to 1 oz.

*P.E.H.C., St. M.H.* (Lotio Calaminæ Oleosa)—Calamine 40 gr., zinc oxide 20 gr., solution of calcium hydroxide 3 dr., olive oil to 1 oz.

*St. T.H.*—Calamine 40 gr., zinc oxide 30 gr., oil of lavender 1 m., solution of calcium hydroxide  $\frac{1}{2}$  oz., arachis oil 225 m.

**Linimentum Calaminæ Compositum (B.P.C.).**

Calamine 43 $\frac{1}{2}$  gr., zinc oxide about 22 gr. and zinc oleostearate about 11 gr. in wool fat, white soft paraffin and liquid paraffin to 1 oz.

**Linimentum Calaminæ Compositum (U.C.H.).** Prepared calamine 9, zinc oxide 5, zinc oleostearate 3, wool fat 3, soft paraffin 20, liquid paraffin to 100.

**Lotio Calaminæ (B.P.C.).**

Calamine about 65 gr. and zinc oxide about 22 gr. with glycerin and rose water to 1 oz.

An excellent slight astringent for itching skin diseases. Used in eczema, especially where the surface is red and tender, also to conceal acne spots on the face. [P2] Mercuric chloride 1 gr. may be added to 6 oz. as antiseptic. For chilblains, sunburn, etc., this lotion or the liniment made double or treble strength, allays the intense irritation.

The following formulæ for calamine lotion are taken from hospital pharmacopœias:—

*C.X.H.*—Calamine 15 gr., zinc oxide 10 gr., glycerin 30 m., solution of calcium hydroxide 80 m., water to 1 oz.

*Gl. Orm. H.*—Zinc oxide 30 gr., calamine 30 gr., glycerin 24 m. solution of calcium hydroxide 24 m., water to 1 oz.

*L.S.H.*—Calamine 20 gr., zinc oxide 20 gr., glycerin 30 m., solution of calcium hydroxide 5 dr., water to 1 oz.

*Mid. H.*—Calamine 30 gr., zinc oxide 20 gr., glycerin 15 m., water to 1 oz.

*P.E.H.C.*—Calamine 40 gr., zinc oxide 20 gr., glycerin 20 m., water to 1 oz.

*St. G.H.*—Calamine 30 gr., zinc oxide 30 gr., glycerin of lead subacetate 5 m., glycerin 30 m., water to 1 oz.

*St. J.H.*—Calamine 20 gr., zinc oxide 20 gr., glycerin 30 m., solution of calcium hydroxide 5 dr., water to 1 oz.

*St. M.H.*—Calamine 30 gr., zinc oxide 30 gr., glycerin 30 m., solution of calcium hydroxide to 1 oz.

*St. T.H.*—Calamine 20 gr., zinc oxide 20 gr., glycerin 24 m., solution of calcium hydroxide 1 dr., water to 1 oz.

*U.C.H.*—Calamine 9, zinc oxide 5, glycerin 3, water to 100.

*W.H.*—Calamine 60 gr., glycerin 10 m., solution of calcium hydroxide 2 dr., water to 1 oz.

**Lot. Calamin. Co. (N.I.F.).** Calamine 3 dr., zinc oxide 3 dr., glycerin 3 dr., solution of calcium hydroxide to 8 oz.

**Lot. Calamin. Oleos. (N.I.F.).** Calamine 180 gr., liquid paraffin 4 oz., oleic acid 20 m., wool fat 35 gr., solution of calcium hydroxide to 8 oz.

### **Unguentum Calaminæ (B.P.C.).**

Calamine 1 in 6 in yellow soft paraffin.

[P1-81] **Unguentum Plumbi cum Calamina (St. G.H.).** *Syn.* ERYSIPELAS DRESSING.

Plaster of lead 3 dr., calamine 20 gr., olive oil 90 m., lard to 480 gr.

**Stannum.** Sn = 118.7. Given internally, pure tin powder is probably not absorbed. Was formerly used as a tænicide. From 4 to 15 g. were given suspended in syrups or made into an electuary and followed in from 3 to 6 hours by a brisk cathartic. Some of the salts (chiefly chloride) are credited with vermifugal properties. In dose of  $\frac{1}{16}$  to  $\frac{1}{2}$  grain the chloride has been used as an antispasmodic in chorea, epilepsy and other convulsive diseases.

**Stanni Oxidum** (Stannic Oxide).  $\text{SnO}_2 = 150.7$ .

*Dose.*—8 to 15 grains (0.5 to 1 g.) daily.

A white or greyish-white powder insoluble in water and hydrochloric acid, soluble in alkalis, forming stannates. Administered for staphylococcal infections. Used chiefly technically and diluted as a cosmetic, e.g., as nail polish.

Distinguish from stannous oxide,  $\text{SnO}$ , which is dark grey—nearly black.

**Tab. Stann. Co. (N.I.F.).** Tin 1.7 gr., tin monoxide 0.3 gr.

**Stanniform (Whiffen, London).** Preparations containing methyl stannic iodide. Available as ointment, dusting powder, lotion and tablets. For treatment of boils, ulcers, carbuncles, whitlows, acne, eczema, burns, chilblains, etc.

**Stannoxylin (Robert et Carrière, Paris; Anglo-French Drug Co., London).**

Preparations of metallic tin, tin oxide or tin salts for the treatment of boils, carbuncles, acne, styes and all staphylococcal infections. Harmless and prompt in action, definite results being obtained in 5 to 6 days. **Tablets** contain metallic tin 42½% and tin oxide 7½%. *Dose.*—4 to 8 daily. May be supplemented by local applications of the following:—**Liquid** contains 25% of tin protochloride. Used as a 2 to 4% solution in water. **Glycerin** contains 2% of the chloride in glycerin. For use in furunculosis of the nasal and aural passages. **Ampoules**, containing equivalent of 0.004 g. of metallic tin in 2 ml., for hypodermic or intramuscular injection. A **Bath** and **Gauze** are also prepared.

**Tin-Ox (John Bell, Hills & Lucas, London).** Combination of tin and tin oxide in tablet form.

**Titani Oxidum.**  $\text{TiO}_2$ . *Syn.* TITANIC OXIDE, TITANIUM DIOXIDE. A white powder insoluble in water, soluble in alkalis and in acids. Used in face powders and other toilet articles in place of zinc oxide.

Titanium salts appear markedly to diminish erythema and pruritus in certain dermatoses. An ointment of the following formula has been found efficacious in a variety of dermatological conditions: titanium salicylate 3, titanium peroxide 5, titanium boric acid 5, titanium oxide 12, titanium tannate 0.1, excipient to 100.

**Siccolum** (*British Drug Houses, London*). A desiccant paste for exudatory dermatoses, containing titanium dioxide, zinc oxide and small quantities of purified silicates in a fat-free base.

## ZINGIBER

*B.P., U.S.P. XI, P. Helv V, Fr. Cx., etc.*

*Dose.*—5 to 15 grains (0.3 to 1 g.).

The dried rhizome (scraped) of *Z. officinale* (Zingiberaceæ).

Must yield not less than 4.5% to alcohol 90%, and not less than 10% to water; *U.S.P. XI* requires minimum of 4.5% to ether. *P.G. VI* has the rhizome not scraped.

*Uses.* Ginger has carminative properties and is sometimes added to purgatives to prevent griping. The tincture is valuable for the relief of acute flatulent distension or colic.

**Fluidextractum Zingiberis** (*U.S.P. XI*). *Average dose.*—10 minims (0.6 ml.). 1 ml. represents 1 g. of ginger, and it contains from 69 to 76% v/v of alcohol.

**Oleoresina Zingiberis** (*B.P.C.*). *Syn.* GINGERIN.

*Dose.*— $\frac{1}{4}$  to 1 grain (0.015 to 0.06 g.).

The acetone-soluble matter of ginger.

**Syrupus Zingiberis** (*B.P.*).

*Dose.*— $\frac{1}{2}$  to 2 drachms (2 to 8 ml.).

Strong tincture of ginger 1, syrup q.s. to produce 20.

**Tinctura Zingiberis Fortis** (*B.P.*). *Syn.* ESSENCE OF GINGER.

*Dose.*—5 to 10 minims (0.3 to 0.6 ml.).

1 in 2 by percolation with alcohol 90%.

**Mist. Zingib. c. Rheo** (*N.I.F.*).

Sodium bicarbonate 10 gr., strong tincture of ginger 2½ m., oil of peppermint ½ m., concentrated infusion of rhubarb 15 m., concentrated compound infusion of gentian 15 m., chloroform water to ½ oz.

**Tinctura Zingiberis Mitis** (*B.P.*). *Syn.* TINCTURA ZINGIBERIS.

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Strong tincture of ginger, 1 in 5, with alcohol 90%.

**Curcuma** (*B.P.C., Fr. Cx.*). *Syn.* TURMERIC ROOT.

The dried rhizome of *C. domestica* (Zingiberaceæ). Used in curry powders and condiments. **Tinctura Curcuma**, 1 in 6, is used as a colouring agent and for the preparation of turmeric paper.

Intravenous injection of curcumin, the pigment contained in turmeric, produces considerable increase of the flow of bile and rapid emptying of the gall-bladder. Clinically, oral administration of preparations containing curcumin shows remarkably good results in chronic cholecystitis.—A. Oppenheimer, *Lancet*, i/1937, 619.

**Zedoary** (*Fr. Cx., P. Jap. V*), the rhizome of *Curcuma Zedoaria* (Zingiberaceæ), resembles ginger in odour and taste.

## VACCINES, SERA, TOXINS AND ANTITOXINS

Preparations made from bacteria, or from the products of bacterial activity, are used for the prophylaxis and treatment of infectious diseases. This form of treatment assists the natural defensive mechanism of the body. It is well known that some people possess an inherent immunity or insusceptibility to certain diseases; this is *natural immunity*. It is also common knowledge that certain diseases, *e.g.*, typhoid fever, scarlet fever and small-pox, rarely attack the same person twice; the first attack has caused the patient to develop a resistance to further attacks; this is *acquired immunity*.

Some bacteria produce during their growth a soluble poison or *toxin*, which can be obtained free from bacteria by filtering a culture through a bacteria-proof filter. A toxin so obtained is known as an *exotoxin* because it is outside, and diffuses readily from, the bacterial cell. Other types of pathogenic bacteria produce no trace of toxin in their cultures, but by grinding up the killed bacterial cells it is often possible to extract substances of a toxic nature from them. This type of toxin which remains attached to the protoplasm of the bacterial cells is termed an *endotoxin*.

If an exotoxin is injected in non-lethal doses, the body develops a certain resistance to it and by repeated injections of small doses of the toxin a considerable immunity can be produced. The substance formed in the blood, which neutralises the toxin, is known as *antitoxin* and is present in the blood serum after the blood cells have been removed by clotting. Such a serum is called *antitoxic serum*.

Similarly, it is possible to produce an immunity to pathogenic bacteria by inoculation into the body of dead or attenuated micro-organisms. The blood serum in this case becomes charged with antibacterial bodies—agglutinins, precipitins, bacteriolysins, etc. and the serum is referred to as an *antibacterial serum*.

It is usual to refer to antitoxic sera as “antitoxins” and to antibacterial sera simply as “sera.” Immunity which is developed by deliberate introduction into the body of bacteria or of their products is known as *artificial active immunity* and is practised in the various forms of prophylactic inoculation. The property of causing the formation of *antibodies* is possessed by a number of substances of a protein character. The general term *antigen* is used to describe any substance which, when injected into the body, will elicit the formation of substances antagonistic to itself. The antigens in common use for the production of artificial active immunity include bacterial vaccines, toxins, toxoids, antiviruses and bacteriophages.

Antitoxins and other antibodies developed in the blood of one individual can be transferred to a second individual by injecting a suitable quantity of the blood or serum containing the antibodies. In this way an immunity can be conferred on the second individual without calling upon his own defensive mechanism. This is



*passive immunity*, but the antibodies do not persist long in the blood of the second individual. Passive immunity is thus only a temporary phenomenon, whereas active immunity is usually of long duration. The antibodies used for temporary passive immunity are usually derived from the serum of horses immunised to the particular infection, and are either antitoxic or antibacterial in effect.

## VACCINES

The ordinary type of bacterial vaccine is a suspension (emulsion) of the killed or attenuated bacteria in normal saline with, as a rule,  $\frac{1}{2}\%$  of phenol or cresol as antiseptic.

Bacterial vaccines may be either (a) **Autogenous**, that is, prepared from cultures of the organisms obtained from the patient, or (b) **Stock vaccines** prepared from stock cultures. Opinions differ as to the relative merits of the two types. For *prophylaxis* it is obviously not possible to have an autogenous vaccine. For *treatment*, autogenous vaccines should, if possible, be used (a) when the infecting agent belongs to an ill-defined group, e.g., *B. coli* infections; (b) when the infection is severe and it is felt to be too great a risk to wait and see whether stock vaccine is effective; (c) when treatment with stock vaccine has failed.

In the case of *B. tuberculosis* an autogenous vaccine is not essential, and there are many obstacles in the way in other diseases, e.g., in gonorrhoea it may be difficult to secure a pure culture, and the loss of time may be of immense importance. In some cases a stock vaccine is used while a special one is being prepared from the case.

Freshly prepared autogenous vaccines are usually to be preferred to stock vaccines. A well-prepared stock vaccine is, however, to be preferred to a badly-prepared autogenous one. Vaccine therapy is of value in the treatment of rheumatoid arthritis, muscular rheumatism, recurrent iritis and other diseases due to focal infection; in staphylococcal infections, in otitis media, chronic sinusitis, unresolved pneumonia, bronchial asthma due to bacterial sensitisation and whooping-cough. Prophylactic immunisation by means of stock vaccines is practised for protection against typhoid fever, cholera, plague, meningococcal meningitis, whooping-cough, etc.—J. A. Kolmer, *J. Med. Soc., N.J.*, 1935, 472.

**Vaccine Therapy** aims at the production of *active immunity* by stimulating the development of specific antibodies within the blood serum of the patient. This action can be used to advantage in the prophylaxis of a number of infectious diseases of which typhoid fever and whooping cough are outstanding examples. Good results also follow the use of vaccines in the treatment of many chronic infections such as furunculosis, bronchitis and streptococcal infections. In pneumonia and gonorrhoea, appropriate vaccines are of value for raising the patient's immunity as an adjunct to chemotherapy.

The results obtained by increasing the power of the defensive mechanism, in other words, by increasing the immunity, are, in combination with sulphapyridine or sulphanilamide, far superior to immunotherapy or chemotherapy alone. The immunity can be increased specifically by vaccines and serums and non-specifically by a great variety of measures.—A. Fleming, *Proc. R. Soc. Med.*, 1939, 32, 911.

**Administration.** Vaccines may be injected into the subcutaneous tissue after the skin has been cleansed with alcohol or other suitable antiseptic. The container should be shaken before the dose of vaccine is withdrawn as the bacterial suspensions settle on standing.

**Doses.** The *prophylactic* doses indicated under the several vaccines in the following pages are suitable for adults in the majority of cases. The *intervals between doses* should usually be 7 days, and may sometimes be extended to 14 days with advantage; in some cases, *e.g.*, whooping cough, when the vaccine is given during the incubation stage of the infection, the intervals should be much shorter—2 or 3 days.

In *treatment*, as regards dose, it is a safe rule to follow that the more acute the infection and the more "toxic" the patient the smaller the initial dose. The doses stated are sufficiently small except possibly in severe generalised infections with marked toxæmia, in which perhaps the dose may be halved. As regards intervals there is no general rule, but the smaller the dose the shorter should be the interval between doses. Thus in septicæmic cases where minimal doses are employed these may be required daily or every other day. Clinical signs, and the focal and general reactions afford the necessary guidance.

The more acute the lesion and the greater the toxæmia of the patient the smaller should be the initial dose; in the case of the more chronic lesions a considerably higher initial dose may be safely used.

**Reactions.** Both localised and general reactions may follow the injection of a vaccine. The local effect is shown by some redness, tenderness, pain or swelling at the site of inoculation, and for an area of 2 to 3 inches around it. The reaction may develop soon after the injection or during the subsequent 24 hours. The general effects may be headache, malaise, slight rise in temperature and pulse rate, and occasionally a rigor. These may develop in about 12 hours and usually pass off within 24 hours.

**Detoxicated Vaccines** (*Research Products, London*). Thomson evolved the idea of treating bacteria, *e.g.*, the gonococcus, with an alkaline solvent, whereby the stroma or bacterial protoplasm and the toxic endotoxin are dissolved. On treatment with acid or acid salt the stroma is again precipitated, the idea being that the toxin is in the solution—the latter is rejected and the bacterial substance, after washing and suspending in slightly acid medium, is used therapeutically.

**Dissolved Vaccines G.L.** (*Glaxo Laboratories, London*). Bacterial cells in solution, a solution of sodium lauryl sulphate 0.025% being the solvent. The surface tension is also reduced, the sodium lauryl sulphate being absorbed by the toxins which are therefore liberated slowly, allowing the production of an adequate supply of antibodies. They are free from reaction and can be given in initial doses of  $\frac{1}{2}$  to 1 ml. for adults, and  $\frac{1}{4}$  ml. for children, subsequent doses in both cases being 1 ml. The following are made: acne and staphylococcus, cold (prophylactic and curative), gonococcus, mixed influenza, staphylococcus, streptococcus, anti-typhoid-paratyphoid, whooping-cough (prophylactic and curative).

**Sensitised Vaccines** (*Sharp & Dohme, London*). *Syn. SEROBACTERINS.* Vaccines which have been treated with the corresponding antisera prior to their use.

The following are made: acne and staphylococcus, cold, coli, combined influenza, gonococcus, whooping-cough, pneumococcus, pneumococcus-streptococcus, staphylococcus, streptococcus, T.A.B.

**Immunogens** (*Parke, Davis, London*). A series of antigens of high activity and relative freedom from bacterial cells and toxins. The following are made: Gonococcus (combined), pertussis, pertussis (combined), pneumococcus, pneumococcus (combined), streptococcus, streptococcus (combined), streptococcus (arthritis).

A type of antigen based upon washing off 24-hour agar growths of the organism with normal saline, agitating to make a homogeneous suspension, and centrifuging. The antigens obtained in the washings are found to be more potent than broth filtrates. The toxic principles are left behind, the washed bacteria being practically as toxic as before treatment. Intramuscular injections thought to be best.

**Phylacogens** (*Parke, Davis, London*) are filtered, sterilised (72 hours) cultures of pathogenic micro-organisms, preserved with phenol 0.5%. The following Phylacogens are supplied: Pneumonia, rheumatism, gonorrhoea, erysipelas, and "mixed infection" (suggested for the treatment of all infections, acute or chronic, in which the condition is not due to a specific micro-organism). Nephritis is a contraindication to their use subcutaneously. Intravenous injection is contraindicated in nephritis, in arteriosclerosis, and in cases with severe and dangerous cardiac involvement. The initial dose should always be given subcutaneously.

**Undenatured Bacterial Antigens** (*Lilly, London*). *Syn.* U.B.A. Represent the natural antigenic complexes of the bacterial cells, are free from metabolites and other non-specific elements and constitute efficient immunising agents. They are standardised on the basis of their nitrogen content. The following are made: Acne mixed, coli mixed, gonococcus, pertussis, respiratory, staphylococcus, streptococcus.

**Local Immunity to Infectious Diseases.** The usual conception of the mechanism of immunity assumes that any change in the immunity level is generalised throughout the body, and that increased immunity brought out in response to stimulation by an antigen is accompanied by the formation of antibodies (antitoxins, precipitins, agglutinins, bacteriolysins, hæmolysins, etc.) in the blood serum.

Besredka claimed that certain tissues have a very low resistance to certain bacteria, though the other tissues may be able to deal with them easily. Hence, he argued, if the weak tissues be immunised the whole animal becomes immune to the infective organism. Thus he claimed that the skin is the weak spot in the case of anthrax, staphylococcus, and other infections, and the gut wall in typhoid, dysentery, etc. If these are immunised by local treatment then the animal becomes immune; he also says this is not accompanied by the formation of antibodies in the circulation.

**Oral Administration of Vaccines.** In accordance with Besredka's theory, the administration of vaccines by mouth has been advocated as an alternative to hypodermic injection. The only conditions in which oral vaccination has met with any measure of success are dysentery and typhoid (*see pp.* 1049, 1088).

A study of the use of dysentery vaccine *per os* was undertaken by the Medical Section of the League of Nations, and comprised the vaccination of 29,880 refugees in camps in Greece. As a result not one person contracted the disease, and in those regions where dysentery was epidemic this method of vaccination completely stopped the epidemics.

After reviewing much of the work done on oral vaccination against enteric fevers, the following conclusions emerge:—(1) On the evidence at present available it is very difficult to maintain that oral vaccination can be seriously considered as an alternative to vaccination by the subcutaneous route. (2) Oral vaccination may, however, be regarded as worth trying when the choice is between this and nothing.—A. Fleming, *Brit. med. J.*, ii/1939, 100.

**Billivaccines** (*La Biotherapie, Paris; Roberts, London*). A series of vaccine preparations in tablets and pills for oral administration. To be taken fasting before breakfast.

**Antiviruses.** Substances of microbic origin capable of local vaccination without the introduction of antibodies. They are selective in their action, and affect only a certain group of cells known as "receptives," e.g., the staphylococcus vaccine has a selective affinity for cells of the skin and certain mucous membranes. *Antivirus dressings* soaked with filtered cultures in bouillon (or a mixture of lanolin and soft paraffin incorporating the antivirus) left in place for 24 hours have been used in a variety of staphylococcal and streptococcal infections, and in many ocular affections, e.g., blepharitis, conjunctivitis, ulceration of the cornea and keratitis.

**Antipeol** (*Medico-Biological Laboratories, London*). Ointment prepared from vaccine filtrates for immunising and cicatrising treatment of sores, burns, and cutaneous infections.

**Antivirin Brand Products** (*Glaxo Laboratories, London*). Sterile detoxicated filtrates of bacterial cultures, including: Staphylococcus Antivirus Liquid, Streptococcus Antivirus Liquid, Mixed Antivirus Jelly (staphylo. and strepto.), *B. acne* Mixed Antivirus Jelly, Antivirus Nasal Jelly (*M. catarrhalis*, etc.).

**Bacterial Antigen Jels** (*Lilly, London*). Dissolved bacterial proteins in a water-soluble jelly base, for local application in various affections, e.g., Colo-Jel, Ento-Jel, Staphylo-Jel, Strepto-Jel.

[P1-S1] **Ophthalmic-Antipeol** (*Medico-Biological Laboratories, London*). Mixed antivirus filtrate with 0.5% Percaine in an ointment base for use in ocular infections.

**Philterterol** (*Astier, Paris; Wilcox, Jozeau, London*). A polyvalent bacteriophage preparation active against *B. coli*, enterococci and staphylococci. Supplied in ampoules containing 3 ml. *Dose*.—One ampoule daily for 10 days. In gastrointestinal affections, staphylococcal infections, etc.

**Propidex** (*Pharmaceutical Specialities (May & Baker) Ltd., London*). A vaccine ointment containing killed bacteria and antivirus of staphylococci, streptococci and *B. pyocyaneus*. For local pyogenic conditions, burns, sores, etc.

[P1] **Rhino-Antipeol** (*Medico-Biological Laboratories, London*). Mixed antivirus filtrate with 3% adrenaline 1 in 1000, 0.5% Novocain, and essential oils in an ointment basis for affections of the nose and throat.

**Bacteriophage.** An ultramicroscopic, filter-passing agent that infects bacteria and can be transmitted from culture to culture. It can only be propagated in living bacterial cultures. By the action of bacteriophage the cultural properties of bacteria and the character of colonies on solid media may be altered; the antigenic properties of the bacteria may be modified and the bacteria are killed or lysed. Organisms most sensitive to the action of bacteriophage are members of the typhoid-dysentery-coli group; less susceptible organisms include the diphtheria bacillus, plague bacillus, staphylococci, streptococci, the bacillus of hæmorrhagic septicæmia and the cholera vibrio. Bacteriophage is extremely stable to heat and chemical reagents; it possesses antigenic properties and various antibodies can be made from it by appropriate manipulation.

The phenomenon of Twort-d'Herelle and its significance.—*Lancet*, ii/1935, 1312.

Use of the bacteriophage in an outbreak of institutional dysentery in a home for blind babies. Ten out of 32 children were affected, but only one further case occurred following administration of antidyserentary bacteriophage three times daily to all the inmates.—*D. Haler, Brit. med. J.*, ii/1938, 698.

**Bacté-Phages** (*Anglo-French Drug Co., London*). Therapeutic bacteriophages for oral and topical administration, e.g., Bacté-Intesti-Phage for intestinal affections, Bacté-Dysenteri-Phage for acute bacillary dysentery, Bacté-Pyo-Phage for purulent affections.

**Bacterial Antigen Lysates** (*Lilly, London*). Solutions of specifically (bacteriophage) dissolved (lysed) bacterial proteins for local and parenteral use, e.g., Colo-Lysate (combined), containing *B. coli*, streptococci, staphylococci and pneumococci proteins; Ento-Lysate, *M. catarrhalis*, pneumococci, *S. aureus* and streptococci; Neiso-Lysate, gonococci, *B. coli*, *S. viridans* and staphylococci; Staphylo-Lysate; Strepto-Lysate, etc.

**Enterofagos** (*Medico-Biological Laboratories, London*). Polyvalent intestinal bacteriophage. For intestinal affections.

### SERA

Therapeutic sera may be (a) normal sera, i.e., the blood serum from healthy animals that have not been subjected to any artificial immunising process, or (b) antitoxic or antibacterial sera, i.e., the blood serum from animals that have developed an immunity in response to injections of a specific antigen (toxin or bacterial suspension), or (c) convalescent or adult immune sera, i.e., the blood serum of human patients who are convalescing from a specific infection or who have had that infection in childhood.

In the *preparation of antitoxin* the antigen used is either the specific toxin or, more usually, the toxoid, i.e., toxin which has been incubated for 4 to 6 weeks at 37° after the addition of 0.2 to 0.4% of formaldehyde. This is injected subcutaneously into the animal, e.g., the horse, with strict aseptic precautions. If unmodified toxin is used it is usually at first mixed with antitoxin, or the animal has a large protective dose of antitoxin given before the inoculation is started. Some reaction, rise in temperature and malaise may occur. Further injections are made at intervals. The quantity injected is gradually increased, and subsequently the injections may be intravenous. The blood is removed from the animal, by the aid of a large sterilised cannula, from the jugular vein; 6 to 12 litres may be collected in sterile flasks. The clot is allowed to form by standing 24 to 48 hours, and the serum is decanted into sterile bottles after the addition of a suitable preservative, e.g., 0.3% of cresol or 0.5% of phenol.

**Refined and Concentrated Antitoxins.** Methods have recently been developed which separate the antitoxin-bearing globulin from those proteins which are devoid of antitoxic value, and which are probably in part responsible for the serum rashes and other untoward reactions which serum therapy may produce in susceptible patients. The precipitation of the globulins containing the antitoxin has led to the production of exceedingly concentrated sera. Thus, whereas a few years ago diphtheria antitoxin contained from 500 to 1000 units per ml., to-day the potency of the refined antitoxin is at least 4000 units per ml.

Fibrinolysin produces a change in the antitoxic pseudoglobulin molecule so that it becomes disaggregated into protein components having different physical and chemical properties. By taking advantage of this property a method of critical differential heat denaturation has been evolved as a method for the further purification of antitoxins. The specific action is not limited to fibrinolysin, but appears to be a property of all the proteolytic enzymes. A process for the large-scale purification of antitoxins has been evolved on this basis, and by using these methods antitoxin of such purity that all the protein present can be specifically precipitated by diphtheria toxin has been prepared experimentally.—C. J. Pope, *Brit. J. Exp. Path.*, 1938, 19, 245.

In the *preparation of antibacterial sera* the antigen used is generally a suspension in normal saline of killed bacteria, and is injected intravenously; sometimes suspensions of live bacteria are used.

**Convalescent sera** are obtained from the blood of convalescent patients and are used for the prevention or modification of measles and whooping-cough and for the treatment of acute anterior poliomyelitis.

**Adult immune sera** are obtained from the blood of adults and are useful when convalescent sera are not available.

The use of immune sera confers only a temporary passive immunity by supplying the patient with ready-formed antibodies (antitoxins or antibacterial substances). Thus in antitoxin treatment a serum which already contains the antitoxin is introduced into the patient's circulation, and has the power of combining with the toxin produced by the infecting bacteria to form an inert substance. (Compare Vaccine Therapy, p. 1023, which confers active immunity.)

**Serum Normale (B.P.C.).** *Syn.* NORMAL HORSE SERUM.

*Dose.*—150 to 300 minims (10 to 20 ml.).

Normal serum is obtained from healthy horses. The blood is withdrawn from the jugular vein and, after it has clotted, the serum is collected, a preservative is added, and the serum filtered through a bacteria-proof filter. The product is tested for sterility and for freedom from toxicity.

**Uses.** It is employed locally, internally and subcutaneously in the treatment of hæmorrhage from wounds, etc., the bleeding of hæmophiliacs, and for hæmorrhage from gastric and duodenal ulcers. For the latter it is given orally 3 or 4 times daily, directly after food, in  $\frac{1}{2}$  ounce of water. 60 or 80 ml. may be given in 24 hours. The serum must be fresh—if it does not produce a good reaction in 24 to 36 hours it is useless for the purpose. Those who have previously received an injection of horse serum may be hypersensitive to it. Symptoms, which may include urticarial eruptions, oedema and other signs of anaphylaxis, usually appear 8 to 14 days after treatment but may appear in a few hours. They may be prevented by injecting adrenaline solution.

**Antilusin** (*Allen & Hanburys, London*) "A" for use *per os* (*dose.*—10 ml. in milk or water 1 to 3 times daily directly after meals), and Antilusin "B" for local application, are preparations of normal serum.

**Byno-plasma** (*Allen & Hanburys, London*) contains 1 drachm of sheep's plasma in every  $\frac{1}{2}$  ounce. For use in convalescence and debility. *Dose.*— $\frac{1}{4}$  to 2 drachms.

**Hemostyl** (*Roussel Laboratories, London*). Fresh hæmopoietic horse serum. In ampoules for oral administration, or as a syrup.

### Thromboplastin.

This name is applied to a substance, derived from blood-platelets, blood cells or tissue cells, which initiates the changes that lead to the formation of the blood clot. According to Howell, thromboplastin acts by liberating prothrombin from combination with an "inhibiting substance"; in the presence of calcium ions the prothrombin is then converted into thrombin and this in turn acts on fibrinogen, converting it into fibrin, the solid substance of the blood clot. Thromboplastin contains the phosphatid cephalin (kephalin); it is soluble in ether, but insoluble in alcohol and acetone. In solution or in solid form cephalin slowly loses its power of hastening the clotting of blood.

Preparations containing thromboplastin are used as hæmostatics for local application to bleeding surfaces. Sterile preparations may be injected subcutaneously or intramuscularly.

**Coagulen-Ciba** (*Ciba, Horsham*). Described as a physiological hæmostatic derived from normal bovine blood platelets, supplied as a powder mixed with sugar to ensure ready solubility, and also in 3% solution in ampoules. May be sterilised by boiling. Administered intramuscularly, orally, or locally (3 to 5% solution); may be given very slowly intravenously in emergency. *Dose.*—Up to 20 ml. of 3% solution.

**Hemagulen** (*Lilly, London*). A physiological hæmostatic prepared from fresh brain substance. For topical application to capillary hæmorrhages.

**Hemoplastin** (*Parke, Davis, London*). Solution of prothrombin and thrombokinase for use as a hæmostatic. *Dose.*—2 ml. injected subcutaneously and repeated every 4 to 6 hours until hæmorrhage controlled.

**Thrombin Coagulant** (*Maw, London*). A stable preparation of thrombin stated to reduce the clotting time of shed blood from the normal period of 6 to 8 minutes to about 15 seconds. The thrombin is dissolved in sterile saline when required for use and applied to the wound on cotton-wool. Dressings impregnated with thrombin are also prepared.

**Hirudin.** *Syn.* LEECH EXTRACT. An active principle from leeches, obtained by treating the minced heads with warm normal saline. *Dose.*—Intravenously, 0.02 to 0.3 g. in 50 ml. of normal saline. Solutions must be freshly prepared. It has the property of maintaining blood in a fluid condition—1 mg. may be dissolved in 0.25 ml. of normal saline for the purpose—this quantity will prevent 7.5 ml. of blood from coagulating without otherwise altering its composition.

European leeches are varieties of *Hirudo medicinalis*. *H. quinquestriata*, the five-striped Australian leech, is used in Australasia.

Repeated injections of hirudin into rabbits makes their blood resistant to the ordinary anticoagulative effects of this substance. The serum of animals thus immunised, when added to blood from other animals, accelerates coagulation. The action of this immune serum on coagulation is much more powerful than the action of normal serum. Smaller quantities can therefore be used and troublesome secondary effects are less likely.—O. Országh and J. Alföldy, *Lancet*, i/1940, 28.

## TOXINS AND TOXOIDS

A number of pathogenic bacteria when grown in artificial fluid culture media excrete into the media poisonous substances or

toxins. Other bacteria, whilst undoubtedly producing toxins, do not excrete them into the surrounding medium, but retain them within the bacterial cell. Toxins of the first type, *e.g.*, those of tetanus and diphtheria, are termed extra-cellular soluble toxins, or exotoxins. Toxins of the second type, *e.g.*, those of typhoid and plague, which are apparently inherent in the bacterial cell, are termed endotoxins.

Exotoxins when injected into animals cause the development of antitoxins in the blood serum. When an exotoxin is treated with formaldehyde solution it is converted into toxoid; by this change it loses its toxicity but retains its antigenic property. Anti-endotoxins are not easily produced, but are present in some antibacterial sera.

The toxins of the diphtheria bacillus and of the scarlet-fever streptococcus are used in dilute solution for diagnostic skin tests. The toxoids of diphtheria and tetanus are used for producing active immunity.

### THERAPEUTIC USES OF BACTERIAL PRODUCTS

*The various vaccines, sera, etc., described in the following pages are classified as far as possible under the diseases in connection with which they are used.*

#### **Acne.**

The acne bacillus may alone be the cause of acne, especially of the non-pustular forms; in the majority of cases, however, it is associated with a staphylococcus. In those cases, in which the acne bacillus is found, the use of acne vaccine may give good results, especially in the cystic form and in acne indurata.

**Acne Bacillus Vaccine** is indicated in the above cases where comedones are the principal features. Combination with polyvalent staphylococcus vaccine may be advisable.

*Initial dose.*—5 millions; then increasing doses—a final dose of 500 millions may be wanted. The interval between doses is 7 to 10 days.

**Acne Bacillus and Staphylococcus Mixed Vaccine** is prepared from both these micro-organisms in various proportions. Some convenient ratios are the following quantities in each ml. Acne 5 millions with staphylo. 100 and 250 millions; acne 10 millions with staphylo. 250, 500, 1000 and 2000 millions; acne 20 millions with staphylo. 2000 millions.

*For cultivation of the bacillus and preparation of vaccine see Vol. II.*

**Anthrax.** Human anthrax is not a common disease in Great Britain. Three clinical forms are recognised. A malignant pustule may appear in the skin or in the alimentary canal, or the bacilli may be inhaled and infect the lungs. Serum is more useful in the



cutaneous form; recovery from the alimentary and pulmonary forms is rare.

**Anti-Anthrax Serum.** *Syn.* SERUM ANTICARBUNCOSUM (*F.E. VIII*), SUERO ANTICARBUNCOSO.

An antibacterial serum prepared by the immunisation of horses, mules or asses with cultures of *B. anthracis*. *F.E. VIII* states preferably from the horse.

**Sclavo's Serum**, obtainable in 10-ml. tubes (from the Jenner Institute for Calf Lymph Ltd., Battersea), is prepared in Italy by immunisation of asses.

*Dose.*—In three or four different parts of the skin of the abdomen, injections of 40 to 80 ml. are given at one time. After 24 hours, if there has been no improvement either in the general or local condition, further injections of 40 to 80 ml. are to be made and repeated next day if necessary. *Begin treatment early.*

Rise in temperature following the injection is favourable. Sometimes a rash develops 3 to 8 days after, with or without febrile symptoms; it is unimportant. The serum keeps for 2 years in the dark—a slight deposit is negligible.

For intravenous injection in severe cases 10 ml. or more, repeated after 2 or 3 hours if necessary.

Mortality from malignant pustule (a variety of external anthrax) reduced in Italy to 5.3% since the introduction of treatment by anti-anthrax serum.—*Brit. med. J. Ept.*, i/1926, 42.

Anti-anthrax serum alone, *i.e.*, without surgical excision of the local lesion, is the treatment of choice. 50 to 100 ml. are given intravenously, and the injections continued daily until temperature drops to normal. It is best to begin with 50 ml. normal saline solution containing 5 drops of serum. Also of value prophylactically in 10-ml. doses subcutaneously.—A. E. Hodgson, *Lancet*, ii/1928, 594.

Anthrax treatment. Serum 80 to 300 ml. as a preliminary, repeated until temperature is normal. "606" in dose of 0.9 g. daily for 3 days, and a fourth dose after a week. Large doses advised.—C. G. Brentnall, *Lancet*, ii/1930, 1174.

At Bradford Royal Infirmary (pulmonary anthrax is still named "maladie de Bradford" in France) excision has now been replaced in most cases by injection of Salvarsan, either alone or combined with Sclavo's serum.—F. W. Eurich, *Brit. med. J.*, ii/1933, 52.

**Bronchitis and Pulmonary Catarrh.** The bacteriology of bronchitis is broadly speaking the same as that of the common cold, except that there is as yet no evidence of a virus infection. The predominant organisms are:—

<i>B. influenzae</i>	present in 40%	<i>M. paratetragenus</i>	present in 23%
<i>Pneumococcus</i>	" " 52%	<i>B. Friedlander group</i>	" " 7%
<i>Streptococcus</i>	" " 53%	<i>B. septus</i>	" " 2%
<i>M. catarrhalis</i>	" " 72%	<i>Streptothrix</i>	" " 3%

(Sputum to be examined after washing out the mouth and throat, and expectorating into a sterile bottle immediately on waking.)

Bronchitis is pre-eminently suited for vaccine therapy—old age and a desperate condition of the patient are not contraindications to treatment.

Autogenous vaccines are more likely to be efficacious than stock ones, and it must be remembered that variation in the flora is liable to occur during the progress of immunisation, hence repeated examination is necessary.

**Catarrh, Nasal and Tracheal (the "Common Cold").**

The etiological agent of the common cold is now generally considered to be a virus. The common pathogenic bacteria, however, present in the posterior nasopharynx, are known to increase in virulence in the presence of influenza and the "common cold," and it is these which are widely held to account for the severity of the symptoms and for the development of complications in individuals whose resistance has been lowered by the virus.

The organisms principally involved—either singly or mixed—in setting up acute catarrhal infections of the respiratory tract are the *B. influenzae*, pneumococci, *B. septus*, streptococci and *M. catarrhalis*, and possibly staphylococci. The organisms appear in cycles. Thus *B. septus* may be found in 80 to 90% of the cases in each epidemic for 2 or 3 successive years and then disappear altogether for 4 or 5 years.

Vaccines for colds, bronchitis, etc., are usually prepared from mixtures of the micro-organisms commonly involved (*vide supra*).

Mixed vaccines containing some or all of the micro-organisms commonly found in infections of the respiratory tract are used for the treatment and prophylaxis of the common cold, bronchitis, influenza, etc. There is considerable variation in the composition and doses of the vaccines used, and, for treatment, the composition of a vaccine may have to be altered to suit prevailing conditions, e.g., when one particular micro-organism predominates in an epidemic.

**Dose.**—For prophylaxis, which is best attempted in late autumn or early winter, three doses of a mixed vaccine are usually given with an interval of 6 or 7 days between each dose. The first dose may be from 100 to 250 millions of the mixed organisms, and the second and third doses may be respectively twice and four times the initial dose.

For treatment smaller doses must be used—from  $\frac{1}{30}$  to  $\frac{1}{2}$  of the prophylactic dose. The more acute the attack, the smaller should be the dose of vaccine. Injections may be repeated at intervals of 3 or 4 days. The earlier treatment is begun the better.

Mixed vaccines of respiratory organisms have proved of value not only in the treatment of catarrhs, acute and chronic, but also in pulmonary phthisis where bronchitic symptoms are conspicuous—in such cases where staphylococci or streptococci are the secondarily infecting organisms they should be included in the vaccine used.

For a period of two years every second child admitted to a home for small children in Stockholm was inoculated with anti-catarrhal vaccine obtained from the State Medical Institution and prepared from strains isolated from patients in children's hospitals and other institutions. Three injections at weekly intervals were given. There were 122 treated children and 125 control children. More than half the number were under observation for three months or longer. No difference in the two groups was found regarding the number of children taking infections, the number of recurrences, the interval between the illnesses, the duration of treatment necessary, or the frequency of complications.—C. Gyllensward, *Acta pædiatr., Stockh.*, 1935, 17, Supp. I, 78.

A carefully controlled study conducted over two years on some hundreds of

University students with three different vaccines recommended for the prevention of colds (normal saline solution hypodermically or lactose capsules being given to the controls) produced no evidence either that vaccines reduce the complications of colds or that the condition of the nose and throat is related to the frequency of colds in a cold-susceptible group.—H. S. Diehl, A. R. Baker and D. W. Cowan, *J. Amer. med. Ass.*, ii/1938, 1168.

One of the factors which has to be taken into account in considering the reasons for the lack of success in the prophylactic use of cold vaccines is the value of the antigen or immunising substance in the vaccine. Every bacterial culture does not necessarily constitute a good vaccine, as has now been shown with a number of different organisms, and there is no doubt that this factor needs consideration when large-scale production of catarrhal vaccines is undertaken. The vaccine is liable to be produced from cultures which have undergone much subcultivation and have thus become liable to antigenic degeneration. At the moment there is no satisfactory means of assessing the value of a catarrhal vaccine, but work has begun and it is probable that in time a vaccine of known immunising power may be produced. At present the best cultures for the purpose are primary or at the most secondary subcultures.—Dennis Embleton, *Practitioner*, 1938, 725.

Vaccine given subcutaneously to 188 persons, intradermally to 95 persons, and 86 controls had placebos. Subcutaneous vaccine reduced the incidence of colds in 74% of persons, and in 6% there were no colds at all. With intradermal vaccine the incidence was reduced in 52.6%, and there were no colds in 11.6%; in the control group, colds were reduced in number in 60.5% and absent in 5.82%.—Hauser and Hauser, per *J. Amer. med. Ass.*, i/1939, 2563.

*Composition of a stock vaccine.* Almost every authority has recommended a different mixture of the vaccine organisms. A vaccine having approximately the following composition has been found very satisfactory: Pneumococci, *H. influenza*, *Streptococcus viridans*, *M. catarrhalis*, and staphylococci, of each 20%. Total bacteria per ml., 500 million.—D. Embleton, *Practitioner*, 1938, 732.

\* **Micrococcus Catarrhalis Vaccine.** A vaccine prepared from *M. catarrhalis* alone is of service in nasal, tracheal and bronchial catarrhs, both acute and chronic, in bronchitis and bronchitic asthma and in catarrh of the middle ear, when the causal relationship of this organism to the attack has been demonstrated.

*Initial dose* of 10 millions may be repeated in 5 to 7 days. In chronic cases 1000 millions or more may be ultimately necessary.

*M. catarrhalis* is one of the constituents of the combined vaccine for colds (see above). *M. catarrhalis* infections may begin at any part of the respiratory tract—characteristically with an inflamed feeling of the fauces and nasopharynx.

Chronic tracheal catarrh is frequently due to infection by this organism or *M. paratuberculosis*, to which secondary infection by staphylococci, streptococci, pneumococci, and other organisms may be added, or by the pneumococcus alone. Cultivations from the trachea showed that non-gram-staining cocci are present in 78% of normal throats and 68% of catarrhal throats.

*M. catarrhalis* is frequently concerned in the causation of common colds, and of influenza, bronchitis, and pneumonia. Causes very irritable cough with scanty viscid expectoration. It grows best on blood-agar, and produces no acid in glucose broth. *B. septus* causes a mild pharyngitis with painful throat, muscular pain, with, however, no temperature and little or no nasal catarrh—probably a common cause of stiff neck and muscular rheumatism. *B. Friedlander* occurs in many acute and chronic colds, and may cause very profuse coryza.

**Directions for taking secretion for preparations of an autogenous vaccine.**

If in the throat, the mouth is washed out in the morning, the throat gargled, and the teeth washed with sterile water; the patient spits once into a sterile bottle. If, on the other hand, the infection is in the nose, the entrance to the nostrils should be washed with soap and water and the discharge blown into a sterilised bottle, or better, post-nasal swabs should be taken.

Autogenous vaccines exerted no influence on the incidence of attacks in 67 individuals suffering from frequent and severe attacks of coryza. A reduction in severity of attacks is the most that can be expected.—L. Hoyle, *Brit. med. J.*, i/1933, 997.

### Oral Cold Vaccine.

It is claimed that when cold vaccines are given by the mouth the soluble antigenic substances penetrate the intestinal mucosa and give rise to antibody formation. Although this is disputed by some workers there is evidence that the vaccines have definite prophylactic value.

A combined vaccine prepared by separately growing Pfeiffer's bacillus, pneumococci (types I to IV), streptococci, and *M. catarrhalis* in broth cultures in bacterial symbiosis with *Anaromyces bronchitica*; when taken for 4 doses ranging from 10 to 20 ml. at weekly intervals, produced in the blood, after the fourth dose, agglutinins for pneumococci in 1 in 40 dilution and for streptococci in 1 in 80 dilution, thus indicating a definite agglutination response after oral administration. No toxic symptoms were observed with these doses at weekly intervals, and it is suggested that this weekly oral dose (swallowed, on an empty stomach, before retiring) can be kept up all the winter without any trouble.—D. Thomson, R. Thomson and E. T. Thompson, *Brit. med. J.*, i/1936, 261.

The oral administration of vaccines for the treatment of colds is based on the observation that heterophile antibodies develop in the blood of rabbits after feeding of heterophile antigen by mouth. Heterophile antibody, often called "Forssman antibody," is a hæmolysin for sheep red blood corpuscles which is produced in rabbits by the injection of many animal tissues and is believed to play a part in resistance to infection. It has been shown that when rats are given pneumococci by mouth they develop an active immunity against pneumococcal infection, and their serum contains protective substances.—V. Ross, *J. Immunol.*, 1934, 27, 235.

In a group of 445 persons oral administration of vaccine reduced the incidence of colds by 43.7% as compared with the control group.—Rockwell and Van Kirk, *Science*, ii/1935, 178.

Clinical tests were made of an oral vaccine consisting of a mixture of bacteria infecting the respiratory tract, the strains selected having a high content of heterophile antigen and also a high resistance to the action of the gastro-intestinal secretions. The cultures were sterilised by heat, the bacteria separated, absorbed on starch, dried and filled into capsules each containing pneumococci 25 billion, *H. influenzae* 5 billion, streptococci 15 billion, and *M. catarrhalis* 5 billion. Tests were made on 100 patients and an equal number of controls. Treated patients took one capsule with cold water at least 30 minutes before breakfast for seven consecutive mornings and thereafter once weekly throughout the season. The treated group showed a decrease of 77.8% in the number of colds, the control group showing a decrease of 10.1%. The latter group had about four times as many colds as those who took the oral vaccine.—G. E. Rockwell, *J. Lab. clin. Med.*, 1937, 22, 912.

After the ingestion of oral vaccines prepared from organisms of the respiratory tract, antibodies cannot be detected in the serum of individuals who have not previously been inoculated subcutaneously.—A. Fleming, *Brit. med. J.*, ii/1939, 100.

**B.D.H. Common Cold Vaccine Tablets** (*British Drug Houses, London*). The vaccine has the following formula: *M. catarrhalis* 4000 million, *H. influenzae* (Pfeiffer) 4000 million, streptococci 8000 million, pneumococci 16,000 million, staphylococci 8000 million, Friedlander's bacillus 4000 million. *Dose*.—One tablet daily for a week, followed by 2 weeks' rest, then one tablet daily for a further week, and then one tablet weekly throughout the winter.

**Entoral (Lilly, London)**. An oral cold vaccine consisting of killed bacterial cultures of pneumococci 25,000 million, *H. influenzae* 5000 million, streptococci 15,000 million, *M. catarrhalis* 5000 million. *Dose*.—1 capsule with a drink of cold water an hour before breakfast for 7 successive mornings and 2 capsules each week throughout the season.

**Genora Cold Vaccine** (*Genatosan, Loughborough*). Vaccine for oral administration containing 2000 million organisms per ml., including *H. influenzae*, *M. catarrhalis*, *Anaromyces bronchitica*, with pneumococci and streptococci. *Dose*.—10 ml. to commence with, taken in water on an empty stomach at bedtime, increasing to 15 to 20 ml. if there is no reaction. Then one dose a week for two months. For the prevention of colds, influenza and pneumonia and for treatment of bronchitis and post-influenzal cough.

**Immunora Cold Vaccine** (*Research Products, London*). A fluid vaccine for oral administration, containing *H. influenzae* (Pfeiffer), influenza streptococcus (Thomson), hæmolytic streptococci, *Aeromyces bronchitica*, pneumococci (several types) and *M. catarrhalis* in 0.25% phenol solution with chloroform water. It contains 2000 million organisms per ml. *Dose*.—The average adult dose is 5 teaspoonfuls to be taken on an empty stomach either the last thing at night or 1 to 2 hours before breakfast. A dose should be taken once a week during winter. A high degree of immunity is stated to be produced after 12 doses.

**Vacagen** (*Sharp & Dohme, London*). Oral cold vaccine in enteric-coated tablets, each tablet containing the soluble antigenic fractions of 60,000 million organisms as follows: pneumococci 25,000 million, streptococci 15,000 million, *H. influenzae* 5000 million, *M. catarrhalis* 5000 million, *Staph. aureus* 5000 million, Friedlander's bacillus 5000 million. *Dose*.—One tablet daily for a week and then one tablet once or twice a week during the winter.

**Cerebrospinal Fever.** *Syn.* CEREBROSPINAL MENINGITIS, MALIGNANT PURPURIC FEVER, PETECHIAL FEVER, SPOTTED FEVER.

A diplococcus, *Diplococcus intracellularis meningitidis* Weichselbaum, has been isolated from the cerebrospinal fluid, and from the brain membrane and the purulent exudate. Four serological types of the meningococcus are known, designated by Gordon's classification types, I, II, III and IV. Serums are prepared by immunising horses to all four types, as well as to individual types.

Griffith's Group I corresponds to Gordon's Types I and III, and Group II corresponds to Gordon's Types II and IV. It has been shown that the meningococcus possesses "rough" and "smooth" variants; "rough" cultures are likely to be less potent antigens than smooth, freshly isolated cultures.—C. G. Rake, *Proc. Soc. exp. Biol., N.Y.*, 1931, 29, 287; G. F. Petrie, *Brit. J. exp. Path.*, 1932, 380; and B. G. Malgraith, *ibid.*, 1933, 227.

Classifications of meningococci worked out in the years 1909 to 1918 represented true serologic relationships which can be plainly recognised to-day. Certain changes in these relationships have taken place; types I and III have become so closely interrelated that separation into two types no longer seems of definite value in practice. This I-III group has become markedly predominant in nearly all parts of the world. On the other hand, types II and IV have, in the United States at least, become entirely distinct from each other so that they do represent two separate groups. There seems to be three types of meningococci, I-III, II and IV. The evidence is that there is a greater number of type II strains in carriers and that this type is especially apt to be responsible for septicæmic and generalised forms of meningococcal infection, which may be relatively mild and chronic. Both the endotoxins of Gordon and the soluble toxins reported by Ferry are produced to a greater extent by the I-III group.—S. E. Branham, *J. Amer. med. Ass.*, i/1937, 692.

**Serum Antimeningococcicum (B.P.C.).** *Syn.* MENINGOKOKKEN-SERUM (*P.G. VI*).

Obtained from the blood of horses immunised to strains of the *Diplococcus intracellularis meningitidis* Weichselbaum, formerly known as *Neisseria meningitidis*. *P.G. VI* requires a titre of 1 : 100 in complement deviation test, and at least 1 : 1000 in bacteriotropic tests. 2-, 4- and 8-fold strengths are also mentioned.

*Dose*.—10 to 30 ml. by intrathecal or intravenous injection.

A dose of 30 ml. or more (except when less than this amount of cerebrospinal fluid can be removed) should be given *intraspinally* by lumbar puncture at the earliest possible moment, and repeated daily for at least 4 days. The amount of the dose should be less than that of the cerebrospinal fluid withdrawn, and the serum

should be warmed to body temperature and injected by the gravity method. In children under 5 it is inadvisable to give more than 10 ml. In severe fulminating cases the dose if possible should be 45 ml. After the injection the patient should lie with head and shoulders low and pelvis raised. It is also used intravenously, and, in severe cases, intracisternally. Up to 50 ml. for children and up to 100 ml. for adults may be administered intravenously every 6 to 12 hours, but intravenous injection should be supplementary to intraspinal injection and not a substitute for it.

**MEMORANDUM ON CEREBROSPINAL FEVER** (Ministry of Health Memo., 234, 1940, H.M.S.O.). According to this memorandum, recent advances in chemotherapy give grounds for hope that the routine use of serum treatment may be dispensed with, even as an adjuvant to chemotherapy. In the fulminating type of case, or if the patient when first seen is nearly comatose, the administration of a suitable serum may be considered. It may be given intrathecally at the first lumbar puncture and a large dose may also be given intravenously. Serum which is more than six months old and has not been kept in cold storage, or which is not known to be specific against the current epidemic strain, is likely to be ineffective. There is evidence that even acute and fulminating cases of the disease have been rapidly cured by chemotherapy without the use of serum at all. On the other hand, although there appears to be no convincing clinical evidence that the use of serum is necessary, even as an adjunct to chemotherapy, some recent animal experiments suggest that better results may be obtained by combining the two forms of treatment.

Use of sulphapyridine with meningococcus antitoxin or sulphapyridine with polyvalent-antimeningococcus serum. Thirteen of fourteen patients recovered.—W. J. Roche and C. J. McSweeney, *Brit. med. J.*, i/1939, 1278.

Serum is now unnecessary even as an adjunct to chemotherapy (sulphanilamide or sulphapyridine). It is expensive and bristles with difficulties, whereas chemotherapy is cheap and relatively easy. Intrathecal administration of serum is often dangerous because of the aseptic meningitis and spinal block which may be produced.—S. Banks, *Lancet*, i/1940, 44.

For references to the use of sulphapyridine and sulphanilamide in cerebrospinal fever, see pp. 946, 962.

**Meningococcus Antitoxin (Ferry).** An antitoxin prepared by the immunisation of animals to polyvalent filtrates of 6 to 8 day hormone-broth cultures of the four Gordon groups of meningococcus after the method of Ferry, Norton and Steele. It is claimed that the clinical manifestations of the disease, its commoner complications, and its mortality rate may all be favourably affected by the timely and proper administration of the antitoxin.

**Dose.**—Dependent on the condition of the patient, the degree of toxæmia, the occurrence of complications and whether child or adult, 60 to 100 ml. in 120 to 200 ml. of normal saline may be administered intravenously (injected slowly). This may be repeated daily if required. These doses may be given intramuscularly, but it is probably a less effective route. Dependent on the same factors and also on the volume of spinal fluid withdrawn, 20 to 40

ml. may be injected intraspinally or intracisternally. This procedure may be repeated daily if required (N.N.R., 1940).

Each of the four types of meningococcus forms, in young broth cultures, a soluble exotoxin which is type specific and also a toxin which is common to all four types. These toxins can be detected by a skin reaction following intradermal injection into the human skin. An antitoxin can be produced in the serum of the horse which is capable of eliminating the skin reaction of the toxin. Experimentally produced cerebrospinal meningitis in monkeys can be cured by intraperitoneal injection of the antitoxin.—N. S. Ferry, J. F. Norton and A. H. Steele, *J. Immunol.*, ii/1931, 293; also N. S. Ferry, *ibid.*, ii/1932, 315, 325, and i/1934, 133.

Treatment of 86 cases with Ferry's antitoxin gave mortality rate of 23.5%, compared with 45.9% for cases treated with anti-meningococcus serum. Doses of 20 to 40 ml. *intraspinally*, 60 to 100 ml. (in twice as much normal saline) intravenously, and repeated daily if necessary, are recommended.—A. H. Hoyne, *J. Amer. med. Ass.*, i/1935, 980.

Four cases of meningococcal meningitis in children showed gratifying and rapid improvement following its use and all made a complete recovery. Administration by the intravenous route is the most advantageous.—J. A. Brocklebank, *Brit. med. J.*, i/1937, 857.

**Meningococcus Toxin.** Active immunisation with meningococcus toxin. By not less than three subcutaneous injections of Ferry's meningococcus toxin, a certain percentage of individuals who give a positive skin test can be immunised. The immunity to one type can be produced by injection of a mixture of toxins of all types.—N. S. Ferry and A. H. Steele, *J. Amer. med. Ass.*, i/1935, 983.

Although for active immunisation against epidemic meningitis a greater antibody-possessing substance is needed, further trial of meningococcus toxin is warranted. It is recommended that inoculation be carried out without a previous skin test.—Kuhns, Kisner and Williams, *J. Amer. med. Ass.*, i/1938, 484.

**A PROPHYLACTIC EXPERIMENT.** A vaccine containing 14 strains of meningococci belonging to Gordon's Types I, II, and III was employed prophylactically during the course of an epidemic of cerebrospinal meningitis in Cyprus. The vaccine was grown for 24 hours on boiled blood serum agar and killed by heat for one hour at 60°C. and sent out at 1000 million organisms per ml. The dosage was  $\frac{1}{2}$  ml. and 1 ml. at ten days' interval, though a larger dosage, e.g., 2000, 4000, 4000 millions at weekly intervals is recommended. Although over 30,000 people were inoculated the authors conclude that for various reasons the experiment was unsatisfactory, and make various suggestions as to how a further experiment should be conducted in order to arrive at more conclusive results.—I. H. Maclean and C. E. Bevan, *Proc. R. Soc. Med.*, 1939, 32, 1551.

### **Cholera.**

The disease is marked by the presence of the *Vibrio cholerae*.

**Anti-Cholera Vaccine.** *Syn.* CHOLERA VIBRIO VACCINE. As an immunising agent only.

**Dose.**—This vaccine usually contains 8000 million dead cholera vibrios per ml. An initial dose of  $\frac{1}{2}$  ml. subcutaneously is followed by a second dose of 1 ml. at an interval of a week. This confers immunity for 5 or 6 months.

Oral vaccines have also been employed prophylactically with some success, but the subcutaneous method is said to give superior results (see A. J. H. Russell, *Bull. Hlth Org.*, L.o.N., 1927).

**Cholera Bacteriophage.** Although there is some evidence to show that cholera bacteriophage may be of definite therapeutic value, some time must elapse before a definite opinion can be given. It is best used in association with the simultaneous administration of hypertonic saline, and thus employed it may be a useful adjuvant. The bacteriophage is given undiluted in 1 drachm

doses every 30 minutes till the symptoms improve, or 5 ml. may be given intravenously with the hypertonic saline. It has also been used prophylactically but the evidence as to its utility is doubtful.

Under grants from the Royal Society and the Indian Research Fund Association, extensive field experiments have been carried out since 1929 by Lt.-Col. J. Morison and Drs. E. M. Rice and B. K. Palchondbury, on the treatment and prevention of cholera by means of bacteriophage. In Nowgang, in the province of Assam, with a population of half a million, the deaths per 10,000, subsequent to distribution of bacteriophage in 1929, were, for 1930, 0.99; for 1931, 0.78; for 1932, 0.46; for 1933, 0.36. The lowest previously recorded rates since 1906 were 1.34 in 1918, 1.42 in 1920, and 1.62 in 1923. There was no recorded period in which the death rate for four consecutive years compared with those for 1930-1933. In an epidemic in Darrang (an adjacent district) the mortality of the group treated with bacteriophage was only half that of the untreated when the bacteriophage was administered within 24 hours.—*Indian J. med. Res.*, April, 1934, per *Brit. med. J.*, ii/1934, 29. See also *Lancet*, ii/1930, 647; *Brit. med. J.*, i/1928, 365.

### Anti-Colon Bacillus Serum.

**Dose.**—10 ml. or more. Is prepared from horses which have been immunised against a number of types of *B. coli* obtained principally from cases of peritonitis and puerperal fever.

The action of this serum is chiefly bactericidal, though it also possesses antitoxic properties.

In acute *B. coli* infection of the kidney, 25 ml. of the serum daily for 3 days has been advised, combined with calcium lactate to avoid rashes, joint pains, etc.

**Colon Bacillus Vaccine** is used in the treatment of post-surgical suppuration in abdominal cases, such as sinuses which refuse to heal after operations upon the appendix, gall-bladder, kidney or intestines; also in bacilluria complicating tubercular cystitis, in the nephritis of pregnancy and in endometritis, when due to infection by *B. coli*. Initial doses of 5 million organisms may be repeated at intervals of 7 to 10 days, and may be gradually increased till 100 millions or more are being given. If the doses employed cause any disturbance of the general conditions, as evidenced by rigors or rise of temperature, this must be taken as indication either of pus under pressure or if not this, for diminished subsequent dosage.

Immunisation of the patient 3 to 4 days prior to abdominal operations, in cases where the presence of pus is suspected, is to be advocated—for this purpose a dose of 500 millions may be employed.

In cases of bacilluria the urine should be kept well alkalised by full doses of sodium citrate or sodium bicarbonate.

Vaccine treatment of *B. coli* infections of the urinary tract has given favourable results.

**Antitoxinum Diphthericum** (*B.P.*, *U.S.P. XI*). *Syn.* SERUM ANTIDIPHThERICUM (*P.G. VI*, *P. Ital. V*, *F.E. VIII*, *P. Belg. IV*, etc.).

Diphtheria antitoxin consists of the serum, or of a preparation of the serum, containing the antitoxic globulins separated from coagulated blood of the horse immunised by inoculation with



diphtheritic toxin, contained in the sterile filtrate from a culture of *C. diphtheriæ* in broth—a surface growth is important. It may consist of the serum, either liquid or dried, or of the antitoxic globulins, either in solution or dried.

The potency is determined by biological assay and is expressed in units.<sup>4</sup> Liquid preparations have a potency of not less than 400 units per ml., and solid preparations a potency of not less than 4000 units per g.

*U.S.P. XI* recognises only the solution of the antitoxic globulins and requires a potency of not less than 500 units per ml. *P.G. VI* includes the liquid or dried serum from horses, mules, oxen and camels. Liquid antitoxin from horses and mules must have a potency of not less than 350 units per ml., that from oxen and camels, only 100 units per ml. The latter is mainly used for prophylaxis. Solid preparations contain not less than 5000 units per g.

*F.E. VIII* describes separately the serum and, with a method of preparation, the antitoxic globulins (*Globulinæ Antidiphthericæ*).

For further details of standard, unit, and method of assay, see *Vol. II*.

It deteriorates rapidly during the first few months after preparation; subsequent rate of deterioration is at the rate of 5 to 10% per annum, if stored at a temperature not above 10°.

**Storage.** Solutions of standard diphtheria antitoxin in 66% glycerol saline were found to lose less than 10% of their potency during six years' storage at -4°; at room temperature a loss of about 23% occurred after 4 years; and at 35° the potency declined to one-half after nine months' storage.—*M. L. Smith, Quart. J. Pharm., 1939, 707.*

**Dose.**—For prophylaxis, 500 to 1000 units should be given to contacts as soon as possible after exposure. This will protect for 14 to 21 days. For treatment, not less than 8000 units intravenously or intramuscularly to be given for any age; larger initial doses, e.g., from 16,000 to 30,000 units, are required when the case has been delayed until the 3rd or 4th day from onset. Warm the antitoxin by standing in water at 40° for 10 minutes. Do not wait for bacteriological diagnosis. Children require as large a dose of antitoxin as adults.

*Intraperitoneal injection* may be employed in advanced cases when intravenous injections cannot be given.

The following scheme is recommended. 1000 to 2000 units intramuscularly for passive immunisation lasting up to 21 days; 2000 to 10,000 units intramuscularly for mild cases; 15,000 to 30,000 units intramuscularly or intravenously, according to severity (the latter route if more than 20,000 units are given); 50,000 to 100,000 units intravenously for the most severe cases. If the intravenous route is contraindicated for any reason in severe forms, the antitoxin should be administered intraperitoneally.—*Report of L.C.C. Departmental Committee, per Brit. med. J., ii/1936, 1266.*

The minimum therapeutic dose of diphtheria antitoxin is 4000 units. This may be considered an adequate dose for small scattered patches confined to the tonsils and of not more than 48 hours' duration. If each tonsil is completely

covered with a patch of membrane 8000 units is an appropriate dose. If the faucial pillars are also involved 10,000 units should be the minimum and if the membrane has extended on to the soft palate not less than 20,000 units should be given. If the membrane extends to the base of the uvula 30,000 units is the minimum dose, and if the uvula is also involved 40,000. Should the membrane have spread to the nasopharynx and nasal discharge be present 60,000 units should be ordered. Any spread of the membrane which occurs after the administration of the first dose of serum calls for more antitoxin, and the second dose should never be smaller than the first. If the disease is of longer than 48 hours' duration when first seen these doses should be substantially increased. In cases of "gravis" diphtheria the minimum total dose should be 120,000 units, the first portion given intramuscularly followed by the balance intravenously in six hours.—C. J. McSweeney, *Practitioner*, i/1939, 701.

**Combined Use of Insulin and Antitoxin.** In toxic cases give a preliminary injection of antitoxin intramuscularly; one hour later make a resting blood-sugar estimation, and inject together intravenously (very slowly at 37°) 32,000 to 100,000 units of antitoxin and 20 g. of dextrose in 50% solution; make further blood-sugar estimations at 1, 1½, and 2 hours after, and if the last figure shows a return to normal give 10 to 30 units of insulin intramuscularly, and subsequently dextrose by mouth or intravenously. Case mortality reduced from 35.9% to 22.5% and noticeable reduction of serum sickness.—E. C. Benn, E. Hughes, and S. Alstead, *Lancet*, i/1932, 281.

Patients experienced relief from physical distress by combined insulin and antitoxin.—H. E. de C. Woodcock, *Lancet*, ii/1932, 884.

Significance of sugar tolerance curves and value of insulin in toxic diphtheria discussed by N. D. Begg and E. H. R. Harries, *Lancet*, i/1935, 480.

**Use of Refined Antitoxins.** Purified antidiphtheria serum containing 27,000 units per g. of protein, prepared by the use of a fibrinolytic enzyme, has two or three times the therapeutic value of native antitoxin.—Pope, *Brit. J. exper. Path.*, 1938, 19, 245.

Experimental studies on guinea-pigs to compare the rates of absorption of diphtheria antitoxin concentrated by enzyme action, and of diphtheria antitoxin concentrated by precipitation with ammonium sulphate, show that the former is absorbed more rapidly, is eliminated more slowly, and will protect against a larger dose of toxin.—Glenny and Llewelyn-Jones, *Jour. Path. Bact.*, 1938, 47, 405.

Concentration of serum by use of enzymes impairs antigenic qualities. Guinea-pigs sensitised with normal horse plasma, immune horse plasma or modified globulins could only exceptionally be shocked with enzyme-digested antitoxin.—Weil, Parfentjev and Bowman, *J. Immunol.*, 1938, 35, 399.

**Untoward Results—Serum Rashes, etc., with Diphtheria Antitoxin.** Higher potencies are now used than formerly, and rashes, pain, and swelling are usually considered to be less frequent. Calcium lactate is said to relieve the rash, pain, etc. The symptoms of diphtheria serum sickness are fever and rash, usually urticaria or a variety of erythema multiforme. Sometimes more unpleasant effects, namely, pains in joints, tendons and fasciæ occur with fever. Asthmatic patients should receive injections with caution, even as prophylactic. Intense itching, subsequently vomiting, has been cured by ½ grain of morphine. Adrenaline hydrochloride solution given hypodermically is also useful in controlling serum rash.

Ephedrine by the mouth is successful in aborting these reactions—one tablet an hour before the injection and one tablet every 8 hours for the next fortnight. For children under 4, tablets containing 0.1 g.; between 4 and 9, 0.2 g.; and between 9 and 15, 0.3 g.—P. Paul Levy, *Brit. med. J.*, ii/1933, 354.

An analysis of 4935 cases treated with concentrated diphtheria antitoxin showed that general reactions developed in 17.5% of cases; if local reactions and albuminuria are included the percentage is 21.9%. 80% of the serum rashes were urticarial, 10% were erythematous and scarlatiniform. Concentrated horse

serum used for the treatment of diphtheria rarely causes any anxiety on account of possible serious development.—H. M. Davis, *Lancet*, i/1938, 193.

Among 200 patients treated, with refined diphtheria antitoxin (Pope) the death-rate was only 2.5%. No serum rashes were recorded and immediate reactions after intravenous injections were few. The small bulk of the serum caused less discomfort to the patient than ordinary concentrated serum.—A. Hutchison, *Brit. med. J.*, i/1939, 384.

Serum sickness can be prevented by means of serum from persons convalescing from serum sickness. Convalescent human serum can be given safely on the third day after diphtheria antitoxin.—J. Amer. med. Ass., i/1939, 1260.

### **The Tellurite Test for Rapid Diagnosis of Diphtheria.**

Diphtheria bacilli reduce potassium tellurite to a black substance. This chemical test for diphtheria bacilli may be applied to cultures or directly to a membrane in the throat.

A 2% solution of potassium tellurite is prepared, the salt being dissolved in distilled water at a temperature not above 40°C. This solution should not be kept for more than 30 days. A swab dipped into the solution is applied to the membrane or exudate on the patient's throat. If the infection is caused by *C. diphtheriae* the area that has been in contact with the swab is stated to show obvious blackening within 5 to 10 minutes. If not, there should be no change in colour. The tongue should not be touched and the throat should not have been recently treated with hydrogen peroxide, tannic acid or methylene blue.

In 72 out of 75 cases complete agreement was reached between the results of this bedside method and the bacteriological diagnosis in the laboratory. A. Manzullo, per *Brit. med. J.*, ii/1938, 1152.

Accuracy of the test confirmed (100%) in 44 cases. It is unlikely that any case of diphtheria would be missed through reliance being placed on the test, but the test can in no way take the place of the clinical and bacteriological methods of diagnosis already in use.—E. Tomlin, *Brit. med. J.*, i/1939, 1273.

With careful application a negative finding affords presumptive evidence against diphtheria, but a positive finding does not establish the diagnosis. Though the test possesses a certain value it cannot replace clinical diagnosis, either alone or supplemented by cultural methods.—J. B. L. Tomblinson and R. M. Campbell, *Brit. med. J.*, i/1939, 1275.

The test cannot be depended upon entirely as it apparently misses approximately one case in six and may give false positives.—*Brit. med. J.*, i/1939, 1291.

Many false reactions are given which render the test of little value as an aid to the diagnosis of diphtheria.—K. E. Cooper *et al.*, *Lancet*, ii/1939, 248.

84.3% of the diphtheria cases gave positive results, but on the other hand 36.6% of non-diphtheritic cases also gave positive results. With such a high percentage of error in each direction it seems unlikely that the test is of any practical value.—J. F. Murray, *S. Afr. med. J.*, 1939, 787.

**Diphtheria Carriers** are found of all ages and of either sex; the presence or absence of an obvious pathological condition is no criterion for detecting a carrier, or of virulence. The length of carrier life seems to have no effect on virulence—bacilli have been demonstrated to be virulent after 4 to 8 months in the ear and nose of different individuals. Artificial immunisation under certain conditions may increase the number of virulent carriers, especially when only partially carried out in a community.

**Schick Test in Diphtheria** (introduced by Prof. B. Schick, of Vienna, in 1913). Schick test toxin is injected into the skin to discover whether a person is immune or susceptible to diphtheria. If his blood contains antitoxin, so that he is immune, this antitoxin

prevents the injected toxin from causing a skin reaction. If his blood contains no antitoxin, or insufficient for protection, a circumscribed area of redness about  $\frac{1}{2}$  in. or 1 in. or more in diameter (which may not appear until the third day), persisting 7 to 10 days, is produced, and on fading shows superficial scaling and persistent brownish pigmentation.

**Schick Test Toxin.** A standard diphtheria toxin is diluted so that 0.2 ml. contains the test dose. To ensure that the toxin injected is harmless, B.P. requires that when it is diluted 50 times, 0.2 ml. must cause no reaction when injected into the skin of a guinea-pig, but when diluted 25 times, this dose must cause a reaction. Now the test toxin also contains toxoid which produces no skin reaction but combines with antitoxin. Tests are therefore required to ensure that the test toxin contains a normal amount of toxoid, neither unusually large nor unusually small. The first test requires that 1 ml. Schick toxin mixed with 1 ml. of a dilution containing  $\frac{1}{50}$  of a unit of antitoxin, must give a reaction on the skin of a guinea-pig when 0.2 ml. is injected. This test ensures that the amount of toxoid present is not unusually small, for, if it were, a person might appear immune who in fact had a very small amount of circulating antitoxin. The second test requires that 1 ml. of Schick toxin mixed with 1 ml. of a dilution containing  $\frac{1}{100}$  of a unit of antitoxin must give no reaction when 0.2 ml. is injected into the skin of a guinea-pig. This test ensures that the amount of toxoid present is not unusually large, for, if it were, a person might appear susceptible who had a fair amount of circulating antitoxin. The diluting fluid may be either a sterile solution of sodium chloride, so that the diluted liquid is isotonic with the blood, or may be a sterile solution containing 1.5% v/v of a mixture of 57 g. of borax, 85 g. of boric acid and 99 g. of sodium chloride.

The improvement in methods of making dilutions of diphtheria toxin used in the Schick test has steadily increased their stability during the past sixteen years and now such dilutions remain unaltered for at least six to twelve months or more, at room temperature. 0.1% Witte peptone in borate buffer solution has been found sufficient to stabilise Schick toxin so that it would remain of full potency for twelve months. Recent reports, however, show that in a very small percentage of cases the peptone may give rise to severe allergic reactions. It is now proposed that human serum should be used as a stabilising agent free from this disadvantage, since it has been shown by animal experiments to be a suitable substitute. A 1 in 500 human serum in borate buffer solution will remain stable for six months at room temperature.—A. T. Glenny and M. E. Stevens, *Brit. med. J.*, 1/1937, 709.

**Allergic Reactions to the Schick Test.** Report of 14 cases and treatment with 0.5 to 1 ml. of adrenaline chloride solution 1:1000. "In view of the rarity of the hypersensitive state, practitioners need not be unduly alarmed, nor hesitate to perform a Schick test where indicated. The worst of the reactions caused some anxiety for a time, but the subjects soon recovered completely."—H. J. Parish, *Lancet*, ii/1936, 310.

**Method of Conducting the Test.** 0.2 ml. of the standardised diluted diphtheria toxin is injected intracutaneously into the left forearm. A similar amount of control, i.e., toxin which has been heated, is injected into the right arm. A flush, sometimes with a

deeper red centre, on the site of injection into the left arm, and the absence of an identical flush on the right arm, indicates a positive reaction. This develops in from 24 to 72 hours and is more easily read on or after the third day.

The control test serves to eliminate *pseudo reactions* due to the presence in the test toxin of some substance which is more stable than the specific toxin and which causes reactions in sensitised individuals.

The results of Schick tests may be distorted by the use of tuberculin syringes insufficiently cleansed. Tuberculin has an extraordinary power of adherence to glass and ordinary methods of sterilisation fail to remove it. It is not generally realised that an apparently healthy person may give a vivid tuberculin reaction to a minute dose of tuberculin, e.g., 0.1 ml. of a dilution of 1 in 50,000 or even 1 in 100,000, and false "positive Schick reactions" have been shown to arise from this cause. It is safer to use separate syringes for different dilutions of tuberculin or to employ previously unused syringes wherever there is a possibility of confusion between tests.—*Brit. med. J.*, ii/1937, 670.

**Diphtheria Prophylactic.** The B.P. '32 includes five forms of Diphtheria Prophylactic (Toxinum Diphthericum Detoxicatum). A sixth variety (alum precipitated toxoid) is recognised by B.P. Add. I.

(a) **Diphtheria Toxin-Antitoxin Mixture**, prepared by adding diphtheria antitoxin to a filtrate of a culture on nutrient broth of *C. diphtheriæ*.

(b) **Diphtheria Toxoid or Anatoxin** (F.T.—Formol Toxoid), prepared by treating the filtrate with formaldehyde.

(c) **Diphtheria Toxoid-Antitoxin Mixture** (T.A.M.), prepared by treating the filtrate with formaldehyde and adding a small quantity of diphtheria antitoxin.

(d) **Diphtheria Toxin-Antitoxin Floccules**, prepared by adding diphtheria antitoxin to the filtrate in the proportion necessary to produce suitable flocculation, separating the floccules and washing and suspending them in physiological solution of sodium chloride.

(e) **Diphtheria Toxoid-Antitoxin Floccules** (T.A.F.), prepared by treating the filtrate with formaldehyde and then proceeding as for toxin-antitoxin floccules.

(f) **Alum Precipitated Toxoid** (A.P.T.), prepared by treating the filtrate with formaldehyde, adding alum in the proportion necessary to produce a suitable precipitate, separating the precipitate and washing and suspending it in physiological solution of sodium chloride.

All forms of diphtheria prophylactic are submitted to a test to ensure freedom from toxicity which consists in injecting 5 ml. into each of 5 healthy guinea-pigs, and in seeing that none die within 6 days. Hence, 1 ml., which is the amount injected into a person, must contain less than one-fifth of the fatal dose for a guinea-pig. Further, if any of the guinea-pigs die later than 6 days, a second test is applied in which 1 ml. is injected into each of 5 more guinea-pigs. None of these guinea-pigs must die within 30 days. There are also tests to ensure efficiency.

*B.P. Add. I* includes the following tests:—A quantity not exceeding 5 times the adult dose is injected once, or one-tenth the adult dose is injected twice, with an interval of not more than 4 weeks, into each of not less than 10 guinea-pigs. The immunity produced is such that not more than 2 out of the 10 (or 25% if more than 10 were used) are Schick-positive. For the toxin-antitoxin floccules and toxoid-antitoxin floccules an alternative test is to carry out the above immunisation with prophylactic on not less than 9 guinea-pigs and then to inject each animal twice, at different sites, with one test dose and two test doses, respectively, of Schick test toxin. A positive reaction to one test dose must not occur in more than one-third of the guinea-pigs and a positive reaction to two test doses must not occur in more than two-thirds. This part of the test is carried out not later than six weeks after the single injection of prophylactic or not later than three weeks after the second of the two injections.

Diphtheria toxin-antitoxin, which was the original form of prophylactic used, has been largely displaced by a preparation of diphtheria toxoid. Injections of toxin-antitoxin may be attended with some danger. Some fatalities have been ascribed to freezing of the mixture which destroys the antitoxin, leaving excess of the toxin. The toxin-antitoxin mixture should not be used after exposure to a temperature below 0°. The addition of formaldehyde renders the toxin non-toxic. (The anatoxin is stable for long periods below 20° and resists heating for 1 hour at 65° to 70°). It is not advisable to attempt immunisation in patients with advanced heart disease and kidney affection, or those recovering from acute infectious diseases. It is claimed that 70 to 90% of those treated are found to be immune after 8 weeks. From 1 to 5 years is the most favourable age for diphtheria prophylaxis.

**Immunisation.** Patients who give a positive Schick reaction should be immunised by *diphtheria prophylactic*, of which usually 3 injections of 1 ml. each are given at intervals of 7 to 14 days.

Babies up to 6 months seem to be immune; between the ages of 6 months and 5 years the majority give a positive reaction, and for children within these age limits the test is often considered unnecessary, and the children may be immunised without previous Schick testing.

**Immunisation Against Diphtheria (Instructions by the Ministry of Health).** The Ministry of Health have issued to county councils and sanitary authorities a revised edition of the official memorandum (Memo. 170/Med.) on the Production of Artificial Immunity against Diphtheria. While various forms of diphtheria prophylactic are available for use, all must satisfy the requirements of the Therapeutic Substances Regulations as regards immunising potency and freedom from toxicity. Those mainly used are:—A.P.T., F.T., T.A.F., T.A.M.

It is now generally agreed that in routine immunisation a preliminary Schick test need not be done. If F.T. or A.P.T. is used then in order that any undue sensitiveness may be detected the first dose should not exceed 0.1 or 0.2 ml. If there is undue reaction the initial dose should be repeated, if there is not, then a relatively large dose, say 0.5 ml., should be given. Of T.A.M., T.A.F. or F.T. it is customary to give three doses at two to three weekly intervals, though attempts have been made to reduce the number. For some time much was claimed for the efficacy of one injection of 0.5 ml. of A.P.T. It has been conclusively shown, however, that in children under eight years of age a dose of 0.1 ml. followed in four weeks by one of 0.5 ml. gives much better results. Owing to its relative insolubility and slower rate of absorption a somewhat longer interval is advocated for A.P.T., and it has been suggested that better results would be obtained by increasing the interval between the injections of the other prophylactics also to four weeks. For older children and adults, the first dose of 0.1 ml. serves to detect an unusually sensitive person. Such a person should be given two further similar doses at intervals of two to three weeks or he may be given two doses each of 1 ml. of T.A.F. If the person is not unduly sensitive, the same procedure as advocated for younger children should be followed. In this country and in the U.S.A. the present practice is to use two doses of 0.2 ml. and 0.5 ml. respectively of A.P.T. particularly for young people, though the first dose need not exceed 0.1 ml., while for adults, three doses of 1 ml., 1 ml., and 1.5 ml. of

T.A.F. are commonly employed. In the ordinary routine of immunisation of children, probably A.P.T. will be the prophylactic preferred.

Where protection is urgently required and the necessary tests can be carried out, F.T. is the prophylactic of choice; where, on the other hand, no preliminary testing can be done, where the demands on the Medical Officer's time must be reduced to a minimum and reactions must be avoided even at the cost of somewhat lower immunity less quickly attained, T.A.M. or T.A.F. should be chosen. For nurses and busy adults, T.A.F. should be employed as being less likely to produce local reactions. In all cases the Schick test should be done not less than two months after the last injection. It will usually be found that a few of those who have been given the ordinary course, the number varying from 1 to 10 or 15%, are still susceptible. Such cases should be subjected to a second similar course and again tested not less than four weeks later.

### REFERENCES TO CLINICAL USE OF DIPHTHERIA PROPHYLACTIC.

"The evidence already available leaves no doubt that the disease and its often fatal consequences may now fairly be called avoidable."—J. Graham Forbes, *Spec. Rep. Ser. med. Res. Coun., Lond.*, No. 115, 1927.

Diphtheria, an almost preventable disease, still attacks some 40,000 people every year in England and kills 2000. In a crucial test in the Edinburgh and Birmingham isolation hospitals immunisation virtually abolished diphtheria among the staff and the nurses, constantly and intensely exposed to risk.—W. T. Benson, *Edinb. med. J.*, May, 1934, 293, per *Brit. med. J.*, i/1934, 1081.

Artificial immunisation against diphtheria continues to make uninterrupted progress in this country, although but slowly. Its value is undeniable and is not as yet sufficiently appreciated.—*Rep. med. Offr. Minist. Hlth, Lond.*, 1938.

In New York, in 1936, some 75% of the infant population had been vaccinated. About 1924 this city had annually some 10,000 cases of diphtheria with 700 deaths, but in 1936 the cases had fallen to 1143 with 35 deaths, and in 1938 the reported cases fell to 163. We have nothing like this to show in England; London has only some 5-3% of its child population immunised.—Sir J. C. G. Ledingham, *Brit. med. J.*, ii/1939, 841.

An anti-diphtheria campaign in Montreal progressively reduced the number of cases from 1632 in 1928, with 157 deaths, to 183 cases in 1935, with 21 deaths.—J. Graham Forbes, *Brit. med. J.*, ii/1937, 1209.

(a) **Diphtheria Toxin-antitoxin Mixture.** As already stated, this has now largely been replaced by other forms of prophylactic. For references to its use see previous edition.

(b) **Diphtheria Toxoid or Anatoxin.** Diphtheria toxoid (anatoxin) is a better immunising agent than toxin-antitoxin and may safely be employed in immunising adults. A first dose of 0.5 ml. is given, a second of 1 ml., and a third of 1 ml. to 1.5 ml., with an interval of 14 days between doses. If there is a marked "pseudo reaction" in the Schick test, or a history of diphtheria, give preliminary doses of 0.1 ml. to 0.25 ml. of toxoid.—G. F. Dick and G. H. Dick, *J. Amer. med. Ass.*, i/1929, 1903.

Diphtheria toxoid used for active immunisation without any undesirable local or general reactions. Sensitivity to toxoid demonstrated by intradermal tests. It should replace toxin-antitoxin.—Keller and Harris, *J. Amer. med. Ass.*, i/1934, 2163.

In animal experiments a higher degree of immunity produced by a dose of formal toxoid in 5 ml. of normal saline than by the same dose in 0.5 ml. saline.—P. Hartley, *Brit. J. exp. Path.*, 1935, 468.

**Disappearance of Vaccinating Power.** A subcutaneous injection of anti-serum protected guinea-pigs from death when followed by a lethal dose of toxin 18 days later, but not when the toxin was administered 45 days later. An injection of anatoxin did not protect guinea-pigs from death when inoculated with toxin on the 18th day, but it did protect those inoculated on the 45th day. A dose of antiserum followed  $\frac{1}{2}$  to 8 hours later with one of anatoxin protected animals for 18 days, but not for 45 days. The identical results were observed when the order of administration was reversed. It appears, therefore, that anatoxin was destroyed or rendered ineffective by serum.—A. Besredka, *Compt. rend.*, 1938, 206, 380 per *Amer. J. Pharm.*, 1938, 209.

(c) **Diphtheria Toxoid-antitoxin Mixture.** Review of eight years' work in Birmingham. Since 1927 toxoid-antitoxin mixture has been given in 3 doses of 1 ml. each at fortnightly intervals. Only 14 cases of diphtheria have occurred in 53,000 immunised children.—M. Bard and V. Fellowes, *Lancet*, ii/1934, 1181.

(d) **Diphtheria Toxin-antitoxin Floccules.** The precipitate formed by mixing toxin and antitoxin in equivalent amounts contains all the specific antigen and antibody in the mixture with little non-specific matter.—P. Hartley, *Brit. J. exp. Path.*, 1925-6, 112. Owing to the elimination of much of the non-specific matter, the reaction following injection of floccules is less than that with toxin-antitoxin.

(e) **Diphtheria Toxoid-antitoxin Floccules.** Three injections may be needed. Little likely to produce reactions.—*Brit. med. J.*, i/1931, 757.

Rarely produces reaction in adults and practically never in children.—*Lancet*, i/1935, 229.

Satisfactory results obtained in adults.—D. J. Thomas and N. G. Howell, *Lancet*, i/1935, 579.

Immunisation with one injection of A.P.T. is much less certain in result than three injections of toxoid-antitoxin floccules or toxoid-antitoxin mixture. Of 825 children under 10 treated with A.P.T., 14.55% were Schick positive 12 months later. Of 3673 treated with T.A.F. (or T.A.M.) only 0.9% were Schick positive 12 months later.—H. C. M. Williams, J. D. Dear and W. Stewart, *Brit. med. J.*, ii/1935, 1078.

(f) **Alum-Precipitated Toxoid.** In the immunisation of 1160 school children, in no case was there any constitutional disturbance. A large number showed a very small subcutaneous lump at the site of injection which persisted for some weeks; many showed a slight tenderness, but only of a very trivial nature. Reactions were more numerous in older children, none at all occurring below the age of 10.—J. E. Haine, *Brit. med. J.*, ii/1935, 896.

Injection of 0.1 ml. of alum-precipitated toxoid followed by 0.4 ml. (or less) 3 weeks later, advocated for older children in whom reactions are likely to occur. The small initial dose gives warning if the patient is likely to react to the larger dose of toxoid. 185 children, of whom 20% were over 10 years of age, immunised by this 2-dose method, with only one mild reaction.—Chesney, *Brit. med. J.*, i/1936, 208.

Evidence to show that the 2-dose method gives a better immunity than a single injection representing the same total amount. Of 321 children given one injection only 64% were rendered Schick-negative, whereas of 35 children who received 0.1 ml. and 0.2 ml. 3 weeks apart, all were Schick-negative 15 weeks later.—Parish, *Brit. med. J.*, i/1936, 209.

Several hundred children, all originally Schick-positive and derived from a semi-rural community with an average Schick-negative rate of 13.2%, were given a single dose of 1 ml. of A.P.T. At the end of three months only 37% had become Schick-negative. Another brand of A.P.T. was used as a single dose in the immunisation of several hundred Schick-positive children in a London borough. Of these children 175 were re-tested after 3 months and 20% were found to be still Schick-positive.—G. Bousfield, *Med. Offr.*, 1937, 15.

Two small but well-spaced doses of a reliable alum-precipitated toxoid give a very high rate of "Schick immunity," 99.6% of 1555 children being found to be Schick-negative two months after treatment with two doses of 0.2 and 0.5 ml., given at an interval of four weeks.—G. Chesney, *Lancet*, ii/1938, 587.

The results obtained by some workers with T.A.M. and T.A.F. have varied widely, and those following the use of "one-shot" A.P.T. have been so diverse as to make the method clearly untenable. All the reports of the use of two injections of A.P.T. are in accord with a consistently high Schick-negative rate. The fears of reaction after A.P.T. seem to have been ill-founded. These well-documented facts should go a long way towards giving A.P.T. by two injections a more accredited place in immunisation schemes. This method is now employed in over 40% of schemes investigated, and there is no reason why the other 60% should not have equal confidence in its efficacy.—J. T. Lewis, *Brit. med. J.*, ii/1939, 1226.

Two doses of alum-precipitated toxoid produced the highest antitoxic response in children of any method of immunisation tried.—Volk and Bunney, *Amer. J. Publ. Hlth.*, 1939, 29, 197.

A.P.T. by at least two injections, properly spaced and given in adequate dosage, possesses so many advantages over other antigens that it would be a



misfortune of the greatest magnitude if it should fall into disrepute through wrong technique. The method advocated for use by all authorities responsible for the control of diphtheria is: (1) the dosage should be 0.5 ml. and 0.5 ml. in children under 8 years; in children of 8 years or more the first dose should be 0.25 ml., to be followed by 0.5 ml. if there is no reaction; (2) the interval between the doses to be in no case less than 4 weeks; (3) the injections to be given in opposite arms.—J. T. Lewis, *Brit. med. J.*, i/1940, 728.

**Intranasal immunisation.** A method of actual immunisation against diphtheria by a single subcutaneous injection of purified aluminium hydroxide toxoid, followed by intranasal instillation of purified toxoid dilution. The results, based on quantitative estimations of antitoxin, appeared to be excellent in both rabbits, children and adults, the effect of the intranasal instillations being greatest on those who gave a poor response to the subcutaneous injection. There were no reactions to the intranasal instillations in children, but in adults transitory headache, nausea or fatigue were occasionally experienced. Of the children, 100% developed more than 0.01 unit of antitoxin 6 weeks later, and 96 to 100% developed 0.10 unit or more. Nine months afterwards the immunity appeared to have fallen off considerably, but the response to nasal reimmunisation only, after twelve months, was even better than to the original combined treatment. In the group of 319 probationer nurses, 94% developed more than 0.01 unit and 85% more than 0.10 unit, while 1% were refractory. The method is recommended for adoption for all children without preliminary or control Schick-testing.—Prof. Claus Jensen (Director of the Department of Biological Standards at the State Serum Institute of Copenhagen), per *Lancet*, i/1937, 934.

**Combined Diphtheria and Tetanus Prophylaxis.** A mixture of diphtheria and tetanus toxoids produced a higher antitoxin titre for each infection than that produced by a single antigen. Two doses of the mixed toxoids at two months interval is advocated.—J. V. Cooke, per *Amer. J. Pharm.*, 1938, 209.

Combined alum-precipitated diphtheria and tetanus toxoids in two doses should be used as a routine in pediatrics. A subsequent dose of tetanus toxoid, rather than antitoxin, can be given when there has been risk of infection.—O. L. Von Canon, *Arch. Pediat.*, 1939, 56, 409.

A stimulating dose of the combined diphtheria and tetanus toxoids gives much greater and more durable immunity than two individual injections.—Jones and Moss, *J. Lab. clin. Med.*, 1939, 24, 512.

### Dysentery.

The bacteria causing bacillary dysentery are of two main types—the Shiga and Flexner types of *B. dysenteriae*; the former is prevalent in South-Eastern Europe and Asia, and the latter in Western Europe and North America.

During recent years epidemics of a mild type of dysentery have occurred in Great Britain, the organism responsible being the *Sonne* bacillus, a sub-type of the Flexner group. The disease, which occurs mainly in children, runs a mild course and does not call for the use of antidysentery serum.

**Serum Antidysentericum (Shiga) (B.P.).** *Syn.* SERUM ANTIDYSENTÉRIQUE (*Fr. Cx.*). The serum (or preparation of the serum) of horses that have been immunised to the toxin of Shiga strains of the *B. dysenteriae*.

*For method of standardisation and unit, see Vol. II.*

**Doses.**—Preventive, 4000 units subcutaneously; curative, an initial dose of 8000 to 10,000 units intramuscularly on the outer side of the thigh (into the body of the *vastus externus*), repeated daily till improvement sets in. For a grave case, 10,000 to 20,000 units repeated daily if necessary. Some dilute the dose with 150 to 300 ml. of normal saline and give *intravenously*. In any case, it should be given early. Stools are stated to return to normal

rapidly in successful cases, but treatment must be continued. Pains and temporary rashes may result, which, however, need not alarm.

In fulminating cases large doses should be given; also magnesium sulphate 1 dr. 3 times daily for the first few days. In bad cases morphine may be needed, and for very severe tenesmus a suppository containing cocaine  $\frac{1}{2}$  gr. and iodoform 3 gr. is useful.

It is stated that while much of the endemic dysentery prevailing in tropical and sub-tropical countries is caused by pathogenic amœbæ, epidemic dysentery due to *B. dysenteriae* occurs all over the world, and this bacillus is also found in asylum or institutional dysentery, in some sporadic cases of ulcerative colitis and in certain forms of summer diarrhœa.

**Polyvalent Antidysentery Serum** is prepared by immunising horses to more than one strain—Shiga, Flexner, Sonne and Hiss-Y strains of the *B. dysenteriae*. Only the Shiga antibody can, at present, be assessed in terms of a standard unit.

**Dose.**—In mild cases, 10 ml. intramuscularly at intervals of from 6 to 10 hours if necessary; in severe cases, from 60 to 100 ml., preferably intravenously.

**ULCERATIVE COLITIS.** Believing that the majority of cases of ulcerative colitis are the result of infection with a dysenteric organism, the author has used polyvalent antidysenteric serum in treatment for the past 15 years. After preliminary desensitisation, 20, 40, 60, 80 and 100 ml. of serum are injected intravenously on consecutive days; sometimes a few additional doses of 100 ml. are given. The treatment can only be undertaken safely in a hospital or nursing home, where the patient is under continuous supervision, owing to the possibility of delayed anaphylaxis. If the patient is treated at home 10 ml. of serum should be injected intramuscularly daily for about 10 days; good results are sometimes obtained, although less frequently than with intravenous injections. The great disadvantage of treatment with serum is the possibility of a dangerous reaction. An anaphylactic reaction may occur during the injection of serum, but it is occasionally delayed several hours. Prompt treatment with adrenaline, 1 minim of which should be injected every  $\frac{1}{2}$  minute, after an initial injection of 3 minims, until complete recovery takes place, is almost always effective. Rapid recovery is most likely in the early stages, but it is occasionally very striking, even in the long-standing cases. More frequently the serum produces a certain degree of improvement, with the result that other treatment leads to recovery more rapidly than it otherwise would have done.—A. F. Hurst, *Brit. med. J.*, i/1936, 321.

**Antidysentery Vaccine.** *Syn.* DYSENTERY BACILLUS VACCINE.

*B. dysenteriae* (Shiga) produces in culture a powerful toxin, but the Flexner type does not produce a similar toxin. The presence of this toxin makes it difficult to prepare from Shiga's bacillus a vaccine that can be given in doses large enough to be efficient. From the results which have been obtained by prophylactic vaccines against Shiga's *Bacillus dysenteriae*, there seems to be no doubt that when vaccine is given in sufficiently large doses a considerable degree of immunity results. The extreme toxicity of the vaccine has been countered by combining it with an antitoxic serum or by treating it with chemicals. Both methods seem to furnish a more or less efficient vaccine. It seems likely that the most satisfactory vaccine of this bacillus will be made by treating cultures with formalin.

*B. dysenteriae* (Flexner) includes a number of strains that are antigenically different. A stock vaccine should include representatives of all types. Vaccines of *B. dysenteriae* (Flexner) are practically non-toxic.

**Dose** (of Flexner organisms).—For prophylaxis 250, 500, 1000 millions at intervals of 7 to 10 days. Some give two doses only, 500 and 1000 millions. Initial dose for treatment, 5 to 10 millions.

**Oral Use of Dysentery Vaccine.** Vaccine *per os* reduced morbidity and mortality from dysentery. Both prophylactically and therapeutically as effective as serum: of 3600 men treated in the Rhine Army, none contracted dysentery, while 471 cases occurred in untreated men.—Prof. Besredka, *Lancet*, i/1929, 1092. Criticism by W. F. Harvey, Prof. A. Fleming and others. "Difficult to know what antiviral is."—*ibid.*, 1093, 1157.

Prophylactic oral vaccine reported on favourably in the case of mental patients in an Ontario institution. Flexner strains isolated from patients were grown in broth for 4 days, the organisms killed by heat, and 10 ml. of the suspension of dead organisms in the broth given orally in place of the evening meal on the first day, 20 ml. on each of the next 3 days, and 40 ml. on the sixth day, with no appearance of reactions or inconvenience.—E. P. James and S. G. Chalk, *Canad. med. Ass. J.*, ii/1933, 40.

The literature on oral immunisation against bacillary dysentery is not so extensive nor so conclusive as that on oral typhoid vaccination. Nevertheless, animal experiments and the available statistical reports of immunisation experiments carried out in humans demonstrate the possible value of this method in the prophylaxis of dysentery.—D. Thomson and R. Thomson, *Med. Pr.*, ii/1935, 133.

For details concerning differential diagnosis of bacillary and amœbic dysentery, and other bacteriological data, see Vol. II.

## Gas Gangrene.

A large group of bacteria, the anærobic spore-bearers or genus *Clostridium*, are the cause of the condition known as gas gangrene, of which the most commonly found species are *Cl. Welchii*, (*B. perfringens*), *Cl. œdematiens*, *Cl. septicum* (*Vibrio septicum*), and *Cl. histolyticum*.

It is not possible to say which of the gas gangrene anærobes is the most virulent, but it may be said that *Cl. œdematiens* is mainly toxigenic, *Cl. Welchii* is more toxigenic than invasive, while *Vibrio septicum* is both toxigenic and invasive. Thus, the latter organism may be found in the blood of patients with well-established gas gangrene due to it, whereas the invasion of the blood by *Cl. Welchii* is a late or terminal event.

Antitoxins, both simple and polyvalent, are employed either prophylactically or therapeutically. They may also be employed in association with chemotherapy.

Gas gangrene, like diphtheria, is to be diagnosed principally on clinical evidence which the bacteriologist may or may not be able to confirm, but, as in diphtheria, it would be quite unjustifiable to wait for a bacteriological report in a suspected case, though where mono-specific antitoxins are available for treatment it is an urgent necessity to know the species of the infecting anærobe.

There is no doubt that there exists a synergic action between the drug (sulphapyridine) and antitoxin, for which the most likely explanation is that the antitoxin neutralises the bacterial toxin while the drug exerts a bacteriostatic effect on the organism itself; thus the body's natural defences are able to play their part in completing the destruction of the invader. It would thus be unwise

in any wounded patient in whom gas gangrene is diagnosed or even suspected to withhold treatment with polyvalent antitoxin. It should be given intravenously at the earliest possible moment and in adequate dosage—say one therapeutic dose for the suspected case, and for the established case three to five doses, combined with 6 to 9 g. of sulphapyridine daily until the infection is controlled.—Editorial, *Lancet*, i/1940, 1127.

**Antitoxinum Welchicum (B.P.). GAS GANGRENE ANTITOXIN (PERFRINGENS).**

Prepared from the blood serum of animals immunised by injection of the filtrate from a culture of *Bacillus perfringens* (*Cl. Welchii*). Used either as unconcentrated or concentrated (globulin) serum, either in the liquid form or dried.

**Dose.**—Prophylactic, 4000 units. Therapeutic, 10,000 to 20,000 units intravenously.

**Uses.** Has the property of neutralising the toxin produced by *Cl. Welchii*, and is used for the treatment of wounds infected by this anaerobic organism; also in acute intestinal obstruction and peritonitis, and some cases of puerperal sepsis (e.g., following attempts at criminal abortion).

**INTESTINAL OBSTRUCTION.** Improvement recorded in patients suffering from peritonitis with paralytic obstruction by treatment with *Cl. Welchii* antitoxin. In 54 cases of acute intestinal obstruction treated with antitoxin, mortality rate was 9.3%, as compared with 24.8% in cases not treated with antitoxin. In 256 cases of acute appendicitis treated with antitoxin, mortality rate was 1.2% as compared with 6.3% in control cases.—B. W. Williams, *Lancet*, i/1927, 907; and *Brit. J. Surg.*, 1926, 54.

*Cl. Welchii* serum of real value when gangrenous bowel has to be dealt with, but of no benefit in straightforward cases of simple obstruction.—D. P. D. Willkie, *Brit. med. J.*, ii/1932, 545.

**PUERPERAL SEPSIS.** Gas gangrene antitoxin should be given early in all cases presenting circumstances which may lead to generalised infection, without waiting for bacteriological confirmation of the presence of anaerobic organisms.—A. J. Wrigley, *Proc. R. Soc. Med.*, 1930, 1643.

Recovery in a case of puerperal infection treated with antistreptococcus serum, gas gangrene antitoxin and anticoli serum.—F. Ivens, *Lancet*, i/1929, 606.

Details of a case of gas gangrene infection in a woman who died during parturition.—J. and P. Adams, *Brit. med. J.*, ii/1931, 1179.

**WOUNDS.** Use of polyvalent gas gangrene antitoxin, together with tetanus antitoxin, advised in all cases showing suspicion of gas gangrene.—M. Wiseberg, *Canad. med. Ass. J.*, ii/1932, 278. See also C. H. Fagge, *Brit. med. J.*, i/1930, 50; and D. C. Corry, *Brit. med. J.*, i/1931, 219.

It is considered that the serum should be given early to all wounded men with gross injury of muscle, to all cases in which a large artery is severed, and to all cases in such a state of shock that they must be allowed to resuscitate before an operation is possible. The serum should be polyvalent with the weight thrown on *Cl. Welchii* antitoxin. In the case of established gangrene the serum should be given intravenously and in large doses. It should also be injected into the muscles round the focus and by instillation into the gangrenous focus. The injections should be repeated every few hours intravenously, and locally at every dressing and operation. For prophylaxis the following combined injection is proposed: *Cl. Welchii* antitoxin 3000 units, *Vibrio septique* antitoxin 1500 units, *B. œdemaens* antitoxin 1000 units; this is contained in a dose of approx. 10 ml. For treatment, 2½ times this dose may be given for therapeutic purposes in established cases.—J. R. Army med. Cps, 1940, 74, 92.

**Antitoxinum Œdemaens (B.P. Add. I). GAS GANGRENE ANTITOXIN (ŒDEMATIENS).**

Prepared from the blood serum of animals immunised by injections of the filtrate from a culture of *Clostridium œdemaens*.

Used either as unconcentrated or concentrated (globulin) serum, either in liquid form or dried.

*Dose*.—Prophylactic, 20,000 units. Therapeutic, 50,000 to 100,000 units.

*Uses*. Is injected in the treatment of gas gangrene due to *Clostridium oedematis*. This organism was responsible for about 15% of cases of gas gangrene on the Western front during 1914-18.

**Antitoxinum Vibriosepticum (B.P. Add. I).** GAS GANGRENE ANTITOXIN (VIBRION SEPTIQUE).

Prepared from the blood serum of horses that have been immunised by injections of the filtrate from a culture of the *Clostridium* commonly known as *Vibrio septique* (also known as *B. oedematis maligni*). Used either as unconcentrated or concentrated (globulin) serum, either in the liquid or dried form.

*Dose*.—Prophylactic, 5000 units. Therapeutic, 10,000 to 20,000 units.

*Uses*. *Vibrio septique* is another of the organisms responsible for gas gangrene, and the antitoxin is used for the same purposes as the other gas gangrene antitoxins.

### Gonorrhœa.

**Vaccinum Gonococcicum (B.P.C.).** Prepared from recently isolated cultures of *Micrococcus gonorrhœæ*.

*Dose*.—Gonococcus vaccine is of value for raising the patient's resistance. A dose of 5 million organisms may be gradually increased to 100 millions, injections being given twice weekly.

Opinions differ widely concerning the value of gonococcus vaccine in treatment and concerning dosage. In acute urethritis and such complications as arthritis, prostatitis, vesiculitis, epididymitis, the initial dose may be 5 millions (or less), and by judicious use of the vaccine the duration and severity of the disease may be materially shortened. In chronic cases larger doses up to 500 millions may be given. The diagnostic dose in cases of arthritis of doubtful origin is 500 millions (*vide* Streptococcus Rheumaticus vaccine).

A series of injections will usually free any case of chronic gleet from the gonococcal infection, although it may not succeed in stopping discharge entirely in all cases owing to secondary infections.

Doses may be repeated at intervals of 7 days, and gradually increased until a maximum dose of 500 million organisms has been attained.

The injection of large doses of gonococcal vaccine usually gives rise to a reaction, which may be local or general. The *local reaction* consists in redness and swelling at the site of injection. The *general reaction* is manifested by a rise of temperature accompanied by increased pain and tenderness in the affected joints (in the case of gonorrhœal arthritis). Both reactions usually subside within 24 hours. The reactions are less marked after small than after large doses, and are absent in cases free from gonorrhœa.

In the acute stages of gonorrhœa and cases of uncomplicated chronic urethritis, provided the disease is localised to the urethra, vaccine treatment is unavailing.

Vaccines in suitable doses materially assist the treatment by stimulating the resistance, but they can do harm if given in doses that are too large, particularly at a time when the tissues are coping with large doses of toxin evolved from the infecting micro-organism. The best time to begin vaccine treatment seems to be when the symptoms are abating and the discharge has become no more than a morning gleet.—L. W. Harrison, *British Encyclopædia of Medical Practice*, 1937, Vol. 6, p. 18.

For details concerning the use of gonococcus vaccine in conjunction with the sulphonamides, see pp. 945, 961.

**Arthigon** (*Schering, London*). Polyvalent gonococcal vaccine in a sterile solution of urotropine 40%. Supplied in ampoules of 1 ml., containing doses of from 10 to 1000 million organisms, given either intravenously or intramuscularly.

**Gono-Antipeol** (*Continental Laboratories, London*). Vaccine filtrate of polyvalent gonococci, streptococci, staphylococci and pyocyanus for the prophylaxis and treatment of gonorrhœa. Supplied in bottles of 40 ml.

**Gono-Yatren** (*Bayer Products, London*). Polyvalent gonococcus vaccine preserved in 3% Yatren solution. Given intramuscularly or intravenously in the treatment of chronic gonorrhœa and its complications.

**Gonoderm** (*Parke, Davis, London*). The bouillon filtrate of the gonococcus grown in liquid culture medium—contains the soluble toxin described by Corbus and Ferry. Used by intradermal injection in the treatment of acute, sub-acute and chronic gonorrhœa.

**Toxogon** (*Bayer Products, London*). Concentrated gonococcal vaccine containing 500 to 2000 organisms per ml. for intramuscular or intravenous injection.

**Hay Fever Vaccine.** A solution of grass pollen toxin preserved with 0.5% phenol. Prepared by extracting grass pollen by alternately freezing and thawing the pollen in normal saline. Strength stated in "units." 1 unit is defined as the amount of extract yielded by one-millionth of a gramme of pollen. *Immunisation* should be commenced in susceptible persons during February with an initial dose between 20 and 100 units (depending on the degree of susceptibility as shown by the skin test or eye test). Subsequent doses may be given every 7 or 10 days, cautiously increasing the amount each time. If time is short, doses may be given more frequently—several times a day if necessary. *In treatment* the initial dose may be determined by the ophthalmic reaction, or failing this, give 50 units initially.

Extracts from all grass pollens furnish one and the same antigen for the purpose of desensitisation to hay fever. A patient who is sensitive to one grass pollen is sensitive to all. Timothy grass, *Phleum pratense*, is the pollen to which patients are most sensitive, and desensitisation to this pollen desensitises to all grass pollens.—J. Freeman, *Lancet*, i/1933, 573 and 630.

Best method for immunisation is by long succession of prophylactic doses given in the early spring up to the hay fever season, commencing with a small initial dose of 40 units and gradually rising to as much as 10,000 units. If immunisation is commenced in February, a dose every other day will prove sufficient; if in March, a dose every day, and in May, three, four or even five doses a day. It is always possible to resort to a "rush" course in a hospital, when desensitisation can be completed in a week by cramming eight doses into each day. The most convenient method is to teach the patients to inoculate themselves.—J. Freeman, *Lancet*, ii/1936, 92.

For a consideration of cutaneous tests and non-specific protein therapy in asthma, hay fever and numerous allied affections, see p. 792 et seq.

**Influenza Vaccine.** Influenza vaccines are usually polyvalent, containing the chief types of bacteria found in the catarrhal secretions of the respiratory passages in epidemic influenza, *viz.*, *H. influenzae* (Pfeiffer's bacillus), pneumococci and streptococci.

The influenza bacillus, believed by Pfeiffer to be the cause of epidemic influenza, must now be regarded as a secondary invader, since it has been shown by Smith, Andrewes and Laidlaw (*see* Vol. II) that the primary infecting agent is a filter-passing virus. It is generally recognised, however, that the secondary organisms are responsible for the serious pulmonary complications which so often prove fatal, and on these grounds, therefore, it is reasonable to suppose that the prophylactic use of a mixed influenza vaccine might raise the individual resistance. To be of service the injections should be given before the beginning of the influenza season, *i.e.*, in the early autumn.

A formula which has been widely used consists of *H. influenzae* 400 millions, pneumococci 200 millions, and streptococci 80 millions, in 1 rnl. An initial dose of  $\frac{1}{2}$  ml. is given, followed after an interval of 10 days by 1 ml.

**Whittingham's Influenza Vaccine** (Duncan, Flockhart, Edinburgh). A prophylactic vaccine containing *H. influenzae* 25 mill., pneumococcus 100 mill., streptococcus 50 mill., *M. catarrhalis* 100 mill., pneumobacillus 25 mill. This is the "A" strength; "B" and "C" strengths are also supplied containing respectively twice and four times the number of each of the organisms in "A."

**Influenza Virus Vaccine.** Influenza virus, isolated from cases of human influenza, can be propagated by passage through mice or ferrets, or on the chorioallantoic membrane of developing chick embryo. In preparing vaccines for human use the virus is grown in one of these ways and the living cells removed by filtration. Its potency is measured in terms of the infective dose for mice, and it is inactivated by means of formaldehyde solution.

Protection experiments in mice and ferrets, and antibody production in man and the rabbit, indicate that suspensions of elementary bodies killed by heat at 57° constitute a satisfactory immunising agent against epidemic influenza. Dramatic results are not to be expected from the use of immunising agents to prevent influenza in human beings, but in certain circumstances these should be of definite value.—R. W. Fairbrother, *Lancet*, 1/1938, 1269.

A formalised vaccine made from the lungs and spleens of ferrets suffering from a simultaneous infection with the viruses of influenza and distemper produced a solid immunity in ferrets, associated with a high titre of influenza antibodies. The immunity evoked by the vaccine protects the ferret not only against the strain of influenza present in the vaccine, but also against antigenically unrelated strains. Trials with the composite vaccine in man are proposed.—F. L. Horsfall and E. H. Lennette, *Science*, 1940, 91, 492.

**Epidemic Influenza Virus Suspension I.V.S.** (*British Drug Houses, London*). Epidemic influenza virus inactivated by heat at 57°. *Dose*.—1 ml. subcutaneously. The resulting immunity is stated to last approximately 12 months. As complete immunity is not produced for a few weeks, prophylactic treatment should be given in the autumn.

**Measles.** The ætiology of measles is still unknown, but it is thought to be due to a filter-passing virus.

**Seroprophylaxis.** Good results have attended the use of seroprophylaxis, by means of which either active or passive immunity can be conferred. Except in an ailing or weakly child

the aim should be to attenuate rather than to prevent an attack of measles, since such a procedure will enable the child to gain a lasting immunity; active immunisation is therefore the more important measure.

Immunisation may be achieved by the injection of either (a) convalescent serum, (b) adult serum, (c) parental blood, or placental extract (immune globulin). Certain local authorities have arranged for the collection and issue to practitioners of adult measles serum, and many hospitals, including the hospitals of the Metropolitan Asylums Board, keep supplies of "pooled" convalescent serum ready for use. Immune globulin is available commercially.

A review of the literature would seem to indicate that, from the point of view of effectiveness, there is little to choose between any of these methods, though convalescent serum and immune globulin are perhaps the two most widely used.

**(a) Convalescent Serum.** The blood is collected from convalescents on the seventh to tenth day of normal temperature, and after treatment with Trikresol the serum is stored in an ice-chest.

*Dose.*—From 3 ml. for patients under 1 year, increasing by 1 ml. for each year up to 7 ml. for those over 5, 10 ml. at 10 to 12 years, and 12 to 20 ml. for adults. Its use in infants under 6 months is inadvisable. If complete protection is desired, with passive immunity for 2 to 4 weeks, serum should be given on or before the 5th day of incubation, but if a modified attack is desired the serum should be given between the 6th and 9th days. The injections, which are given intramuscularly, do not cause anaphylaxis or reaction.

Injections of 5 ml., even up to eighth or tenth day of exposure, of great benefit. Complete protection secured in 185 out of 233 patients (80%), whereas 23 out of 32 controls contracted measles.—T. M. Hunter, *Brit. med. J.*, i/1933, 218.

Immune measles serum finds its most brilliant application when administered in the incubation period. Doses of pooled convalescent serum, of from 5 to 20 ml. according to age, given before the fifth or sixth day after earliest ascertained exposure, almost invariably afford complete though temporary protection. If given later in the incubation period, but before the onset of symptoms, attenuation of attack is more likely to follow and should be aimed at in every instance when circumstances permit.—W. Gunn, *Practitioner*, ii/1936, 515.

The intravenous injection of adequate amounts of convalescent serum, if given in the pre-eruptive stage, modifies the course of the measles in most cases. The effective dose is from 40 to 50 ml. given at least one day before the appearance of the eruption. It is especially indicated in weak and debilitated children, in those just recovering from whooping cough and other infectious diseases of childhood, and in those in whom measles has developed during the course of another acute or chronic disease.—J. L. Kohn, *J. Amer. med. Ass.*, ii/1938, 2361.

**(b) Adult Serum.** The blood serum from adults who have had an attack of measles in childhood. The serum is collected under aseptic conditions and stored in an ice-chest, when it will retain its full potency for 6 months. The serum from adults up to 50 years of age is as potent as that from adolescents.

*Dose.*—A dose of 20 ml. is given intramuscularly. If given within the first four days after exposure a mild or attenuated attack may be expected in 80% of those contracting the disease;



if given from the 5th to the 7th day after exposure a mild attack may be expected in 60%. The duration of the partial immunity conferred is at least 10 days and possibly longer.

In the epidemic of 1931-2, during which 11,526 cases were admitted to the L.C.C. Hospitals, comparisons were made of the results obtained with convalescent and adult serums, with the conclusion that 90% prevention was secured by convalescent and nearly 80% by adult serum, and that adult serum used in prevention yielded about 70% better results than those in untreated or control cases. "Adult serum a valuable therapeutic agent which can be used in the treatment of measles on a larger scale than is possible with human convalescent serum."—Rept. of M.O.H. and School M.O. on the Measles Epidemic, 1931-32, *Brit. med. J.*, ii/1933, 830.

Adult serum in a school epidemic of measles. The serum exerted a beneficial effect, as shown by a less severe illness and a diminished incidence of complications in the majority of the inoculated cases, compared with the unprotected cases.—L. R. Lempriere, *Brit. med. J.*, i/1939, 1137.

Normal adult serum has been found to be about one-third as potent as convalescent serum, but is reasonably effective in modifying attacks. The immune globulin from human placentas is not much more effective than adult serum, and reactions sometimes follow its use.—W. Gunn, *Lancet*, ii/1939, 601.

(c) **Parental Blood.** Where there is a difficulty in obtaining convalescent or adult serum, blood may be withdrawn from the vein of either parent (who must, however, have suffered from measles at some previous date) and up to 10 ml. injected forthwith intramuscularly into the exposed child. No anti-coagulant is necessary and there is no risk of anaphylaxis.

The blood of normal adults is a valuable source of antitoxin. While 23 infants left unprotected during an epidemic all suffered from a typical attack, 19 out of 56 injected with 30 ml. of parental blood escaped entirely and the remainder only had a mild attack.—J. M. Lewis and L. H. Barenberg, per *Brit. med. J.*, i/1933, 423.

The injection of whole adult blood has been much less often employed than the alternatives—convalescent serum, adult serum and immune globulin—a fact which is greatly to be deprecated, since it is the most generally applicable, useful, convenient and inexpensive method, and is particularly suitable to private medical practice. Of 20 contacts treated, 4 were completely unaffected, 14 developed modified measles and 2 were failures. The average injection was 10 ml. intramuscularly.—T. D. Culbert, *Brit. med. J.*, ii/1938, 705.

(d) **Immune Globulin (Placental Extract).** A sterile, refined and concentrated preparation of globulins made from human placental blood and tissues, and containing immune factors against measles. The immunising potency of the product is determined on the basis of the diphtheria antitoxin titre of the placental blood. It is said to be equivalent in usefulness to convalescent serum, while being more readily available. The only objection is that reactions, such as pain and redness at the site of injection, rise of temperature, nausea and pallor, may follow its use.

**Dose.**—From 2 to 10 ml. intramuscularly, according to the age of the patient and the intimacy of the contact. The usual doses are: for prevention 2 to 5 ml.; for modification 2 to 10 ml.; for treatment (with caution) 5 to 10 ml.

Doubtful whether the injection of sufficiently large doses to give complete protection is justifiable outside institutions, except in cases of debilitated, tuberculous or other acutely or chronically affected children. Rather the immune globulin should be used to modify the disease and presumably thereby to render the patient permanently immune. American workers are of the opinion that it is at least as effective as the most potent globulin serum.—*Pharm. J.*, i/1936, 739

The advantages and disadvantages of immune globulin (human) as an immunising agent in the prevention and modification of measles are at least equal to those of other preparations which have been used for a similar purpose. Reports seem to be about equally divided on the question of whether or not this immunising agent is superior to convalescent serum. Reactions are not infrequent and not always mild.—Report of the Council on Pharmacy and Chemistry of the A.M.A., *J. Amer. med. Ass.*, ii/1938, 1764.

In an epidemic of measles in a girls' school, immune globulin was used as a prophylactic. There were no serious reactions following the injections. The treatment did not prevent or postpone an attack of measles, but rendered it mild and the duration of fever shorter, and lessened the incidence of complications. The immunity probably diminished rapidly after three weeks.—T. N. Parish, *Brit. med. J.*, ii/1938, 65.

Immune globulin obtained from placentas is considered to be as effective as convalescent serum for the prevention and modification of measles. It remains to be seen to what extent measles can be modified and still allow the development of a permanent immunity such as follows a definite case of measles.—*Int. med. Digest.*, 1939, 34, 189.

**Immune Globulin (Human)** is issued in 2 and 10 ml. vials by *Parke, Davis & Co., London*, and *Lederle Laboratories, New York (C. F. Thackray, Leeds)*.

**Embryonin** (*Bioglan Laboratories, Hertford*). A placental extract in 2 ml. ampoules. Advocated for the prevention and modification of measles.

**Antistreptococcal serum.** It is a matter for doubt whether immune measles serum—convalescent, normal adult, or placental—exerts any specific curative action once the disease is established. The therapeutic results of considerable doses, from 20 to 30 ml., of convalescent serum given intravenously have failed to convince the impartial observer of its value. It is probable that any benefit that may accrue is attributable more to complement and allied bodies, or even to streptococcal antitoxin, in the serum than to a specific anti-measles action. So pronounced are the effects of anti-streptococcal serum in lowering the incidence and severity of complications, the majority of which are due to streptococci, that it is administered almost as a routine in fever hospital practice. Doses varying from 10 to 50 ml. by the intramuscular route usually suffice.—W. Gunn, *Practitioner*, ii/1936, 515.

In the common and fatal broncho-pneumonias and empyemas following measles in camps, *S. hæmolyticus* was found constantly. The importance of carriers of this organism in measles wards cannot be over-estimated. Cole found 11.4% of measles cases carried it on admission, 38.6% after 4 days, and 56.8% after 8 to 16 days.—Stitt.

## Pneumonia.

The organism responsible is the pneumococcus. It has been customary in the past to describe four principal types of pneumococcus—Types I, II, III, and a fourth group, IV, consisting of cocci which do not conform to the characteristics of the other three types. Recent work has shown, however, that this last group contains at least 29 different types (Types IV to XXXII), and that it is this heterogeneous group which is largely responsible for primary broncho-pneumonia. In other words, there are 32 ætiological forms of pneumococcic pneumonia.

The bacteriotherapy of pneumonia may therefore be achieved (a) by the subcutaneous injection of a stock pneumococcus vaccine (or, where possible, of an autogenous or type-specific vaccine), or (b) by the intravenous injection of a type-specific serum.

**Pneumococcus Vaccine.** Prepared from killed cultures of representatives of all the recognised serological types of the pneumococcus, or from one of the types only.

**Dose.**—In the treatment of lobar pneumonia the recommended dose varies widely, an appropriate initial dose (for a monovalent

vaccine) being from 10 to 50 millions, repeated every 24 hours until the temperature falls, though some workers prefer to give a much larger dose, e.g., 100 millions or even more, to abort the attack. If a polyvalent vaccine is used, much larger doses, e.g., up to 1000 millions, may be employed. It should be borne in mind that successful results are only obtained by early administration, preferably not later than the third day of the disease.

Pneumococcus vaccine is also employed in the treatment of chronic and sub-acute localised infections due to the pneumococcus, such as empyema, arthritis, sinusitis, abscesses, etc., and numerous conditions of the respiratory tract in which the pneumococcus is the infecting agent. Frequently other organisms are present in these conditions, e.g., *H. influenzae*, staphylococci, streptococci, etc., giving rise to mixed infections, and in these cases mixed vaccines should be employed.

The percentages of cases of pneumonia due to bacteria other than pneumococcus is probably very much greater than is supposed. This was verified by the experience of the widespread epidemics in 1918-19 of so-called "Spanish flu." In cases where pneumonia is said to supervene upon influenza, the infection is a double one from the beginning, and much may be done to prevent the pneumonic attack by giving doses of 25 to 50 millions of pneumococcus vaccine, combined with 50 to 100 millions of *H. influenzae*, as early as possible during the influenzal attack. Thus, "P.S.I." vaccine, advocated by W. H. Wynn (*see Brit. med. J.*, ii/1934, 1159) contains 200 millions each of pneumococci, streptococci and *H. influenzae*, the initial dose for an adult being 600 millions (1 ml.) and for an infant of one year 20 millions, these doses being repeated at 24-hour intervals.

Opinions are sharply divided as to the value of vaccine therapy (as opposed to serum therapy) in lobar pneumonia, and some workers have condemned it as useless. The special advantages claimed for it by its exponents are that it is easy to apply, requires no special technique, and is without dangerous effect. It is probable that a large percentage of failures with stock vaccines is due to the vaccine not conforming in type with the infecting organism. Stock vaccines must be polyvalent, and polyvalent in each of the types peculiar to the country. Autogenous or type-specific vaccines are clearly preferable.

Method for the rapid production of autogenous vaccine for treatment of pneumonia, with notes on its successful use in nine cases.—F. P. G. de Smidt, *Brit. med. J.*, ii/1938, 1140.

Vaccine treatment appears to be successful in reducing the duration of uncomplicated pneumonia by an average of 3 days. Recovery within five days of the development of pneumonia is much more likely if vaccine has been administered. Some cases respond immediately with crisis and marked improvement of condition.—J. H. Bolton, *Quart. J. Med.*, 1938, 7, 171.

**Prophylactic Use.** In addition to their therapeutic use polyvalent pneumococcus vaccines have also been employed prophylactically with some measure of success in camps, mines, etc.

Sir A. E. Wright found that doses up to 40,000 million produced nothing more than a slight constitutional disturbance and a slight rise in temperature. Lister advises a vaccine of four types, containing 6000 millions per ml. of each type, making a total of 24,000 millions per ml. Of this 1 ml. is given as initial dose, twice repeated, at intervals of 7 days. Borel holds similar views, and he inoculated Senegalese troops in France with initial doses of 32,000 millions without ill effect.

For white races, work of investigators of the Rockefeller Institute shows that initial doses of 1000 millions each of the prevalent strains can be safely used, and that with lower doses full immunity may not be secured. After 7 days, either 1000 or 2000 millions is given, and a further 2000 millions 7 or 14 days later.

The pneumococcus types now included in the prophylactic vaccine employed in the Witwatersrand goldfields are I, II, III, V, VII, XII and XIV. (D. Ordman, per *Lancet*, ii/1938, 579.)

**P.S.I. Vaccine (Evans)** (*Evans, Sons, Lescher & Webb, Liverpool*). Vaccine prepared according to Wynn's formula (*vide supra*) for the treatment of pneumonia. *Dose*.—1 ml. repeated after 24 hours.

**Anti-Pneumococcus Serum.** As already stated, the pneumococci have been classified serologically into 32 types, and successful serum treatment is dependent upon accurate bacteriological type diagnosis, the therapeutic effect of any anti-pneumococcus serum being strictly type-specific. Not only has the incidence of these numerous types in pneumonia been fully studied, but the characteristic features of the disease produced by some of them have been defined, and in every one of the new types so far studied from the therapeutic standpoint, serum treatment has been found effective.

**The Incidence Rate** of the various types of pneumococci varies in different localities and in different years. A compilation of data made in America on many thousand cases showed the type distribution in lobar pneumonia for adults to be approximately 29% for Type I, 17% for Type II, 12% for Type III, 5% for Type IV, 7% for Type V, 2% for Type VI, 6% for Type VII, 8% for Type VIII, and 3% for Type XIV, leaving approximately 11% for other types. It was further found that the type incidence in children and adults is quite different. The incidence of Types II and III in children is extremely low, while Types VI, VII, XII, XIV and XIX are most frequently seen; Type I occurs infrequently as compared with adults. In this country it is generally considered that from 60 to 70% of all cases of lobar pneumonia are either Type I or Type II.

Of the 29 types separated from the group originally known as Type IV, it was found that Types V, VII, VIII and XIV occur with much greater frequency than the others. The mortality in serum treated cases was lower than in those not given serum, especially when the serum was given early in the disease.—M. R. Rosenbluth and M. Block, *Arch. intern. Med.*, 1937, 50, 567.

Type VII pneumococcus present in 6.5% of cases of pneumococcal pneumonia in adults and 2.4% in children.—J. G. M. Bullowa and E. Greenbaum, *Arch. intern. Med.*, 1937, 50, 179.

In over 80% of 102 cases, diagnosis of Type I or Type II pneumococcal pneumonia was made by the Neufeld technique using diagnostic anti-pneumococcus horse serum.—Cruikshank and Montgomery, *Lancet*, i/1938, 217.

**Direct Typing of Pneumococci (The Neufeld Test).** The pneumococcus in sputum undergoes a complete change which is observable microscopically when it is acted upon by a specific serum; there is a visible "swelling" of the capsular zone. By means of this test the type of pneumococcus can be ascertained

within a few minutes. The sputum is emulsified in normal saline solution and successive drops of the preparation are mixed on slides with drops of the type-specific sera (from rabbits). A control consists of a drop of the emulsified sputum mixed with a drop of normal saline. Microscopic examination is facilitated by adding a drop of Löffler's methylene blue to the mixtures; the swollen capsules appear unstained and have a ground-glass appearance.

**Therapeutic Value of Anti-Pneumococcus Serum.** The efficacy of serum treatment in pneumococcal infections due to Types I and II is established beyond doubt, so much so that in certain of the American states an organisation exists to ensure that serum shall be available free of charge for every case of pneumonia requiring it. While the most striking results have been obtained in Types I and II, a considerable reduction in mortality has been shown to follow type-specific serum treatment in Types V, VII, VIII, and XIV. No satisfactory serum is yet available for Type III.

To obtain the best results serum treatment must be given early and in adequate dosage. Though it is sometimes of value in cases treated from the 5th day onwards, the results obtained do not warrant its administration as a routine procedure in such cases. Serum treatment is of particular value in two classes of patients; (a) in people of 40 years of age and over, and (b) where there is an infection of the blood stream. Invasion of the blood stream by pneumococci has a marked adverse effect on prognosis. Type I cases with bacteremia, not treated with serum, have been found to have a mortality rate as high as 80%, compared with a rate of from 25 to 40% in serum-treated cases with bacteremia, and of 5% in serum-treated cases without bacteremia. This underlines the necessity for early treatment in the prevention of bacteremia and other complications.

Within 8 to 24 hours after administration of serum there is usually a marked improvement in the patient. The pulse rate and temperature fall, the toxæmia lessens, and a positive blood culture may become negative.

Analysis of cases of lobar pneumonia with early administration of serum. The following phenomena were observed in patients treated with homologous serum during first 24 to 48 hours: Disease may be completely aborted, temperature, pulse and respiration rate dropping to normal within 12 to 24 hours after administration; improvement in general condition due to disappearance of toxæmia; prevention of spread of infection from one lobe to another and limitation of area in lobe primarily infected; prevention or rapid check of bacteræmia; rapid return of leucocytes to normal.—R. L. Cecil, *Brit. med. J.*, ii/1936, 308.

Specific sero-therapy of pneumonia is not popular because of the expense, difficulties in giving intravenous injections, and the limited facilities for typing the organisms.—R. Cruikshank, *Lancet*, i/1939, 1222.

In the absence of any definite contraindications, patients with lobar pneumonia whose early urine specimens contain pneumococcus polysaccharide are suitable cases for serum therapy.—Cruikshank and Montgomery, *Lancet*, i/1938, 217.

In a total of 120 cases treated with type-specific serum the mortality rate was 3.3%; in 125 cases not treated with serum the mortality rate was 16.8%.—R. Horn, *Arch. intern. Med.*, 1939, 12, 922.

**Reactions Due to Serum Sensitivity.** Anaphylactic reactions may appear almost immediately following an intravenous injection of the serum, or they may be delayed for one or two hours,

or serum sickness may develop after an interval of some days. Before serum is administered it is advisable to enquire into the patient's previous history with regard to asthma (especially horse asthma), hay fever, etc., and to employ one of the undermentioned tests for sensitivity. Even in the presence, however, of a negative history and tests, the greatest care should be taken to give the serum extremely slowly and to have a syringe filled with 1 in 1000 adrenaline solution at hand.

**Ophthalmic Test.** A drop of a 1 in 10 dilution of normal horse serum is dropped into the outer canthus of the conjunctival sac of one eye, the other acting as a control. If the patient is sensitive, itching, watering and reddening of the eye occur within 5 to 10 minutes.

**Intradermal Test.** Inject 0.2 ml. of normal saline into the skin of the volar surface of the forearm, and 2 inches away inject 0.2 ml. of a 1 in 100 dilution of normal horse serum. In positive cases a wheal of at least 10 mm. in diameter, surrounded by a zone of redness, appears in from 5 to 20 minutes.

**Blood Pressure Test** (for rabbit serum). Rabbit serum (*q.v.*) produces a positive intradermal reaction in the majority of normal persons, and when this serum is used sensitivity should be tested by giving an intravenous injection of 0.1 ml. of serum, diluted with 5 ml. of normal saline; if the fall of blood pressure following this does not exceed 15 mm. Hg., and no symptoms of shock appear within 5 minutes, the patient may be considered non-sensitive.

**Serum Antipneumococcicum I (B.P. Add. I).** *Syn.* ANTIPNEUMOCOCCUS SERUM (TYPE I). Prepared from the blood serum of animals immunised by injections of cultures of *Diplococcus pneumoniae* Type I. Used either as unconcentrated or concentrated (globulin) serum, either in the dried or liquid state.

*Dose.*—50,000 to 150,000 units intravenously.

**Serum Antipneumococcicum II (B.P. Add. I).** *Syn.* ANTIPNEUMOCOCCUS SERUM (TYPE II). Is similar to the preceding, except that the cultures used for immunising the animals are of pneumococcus Type II.

*Dose.*—50,000 to 150,000 units intravenously.

The first injection should be made cautiously and slowly, and the ampoule should be warmed to blood-heat beforehand. If there are any signs of collapse or urgent dyspnoea after the injection, from  $\frac{1}{2}$  to 1 ml. of a 1 in 1000 solution of adrenaline should be injected subcutaneously.

Since from 60 to 70% of all cases of lobar pneumonia are either Type I or Type II, a duovalent serum has often been given during the 24 hours which used to elapse before the bacteriologist's report was available. With the Neufeld method of rapid typing, however, the type of pneumococcus can be identified within an hour, and where facilities exist for the use of this method the use of duovalent serum is unnecessary and uneconomical.

**Felton's Serum.** This is a concentrated and refined serum in which the antibody-containing globulins are precipitated by dilution with distilled water or weakly acid buffer solutions (*see* L. D. Felton, *J. infect. Dis.*, Dec., 1928, 543). By the use of this serum it is possible to give an effective dose intravenously in comparatively small bulk, and with a consequent reduction in the frequency and

severity of the reactions due to the protein content. The concentrated serum is stated to be from five to ten times as potent as the unrefined serum, an initial dose of 10,000 Felton units being the equivalent of 50,000 units of the unrefined serum.

In 1934 the Therapeutic Trials Committee of the M.R.C. issued an authoritative report on the use of this serum, based on observations on 1375 cases treated during 1930 to 1933 in Aberdeen, Edinburgh, London and Glasgow (*see Brit. med. J.*, i/1934, 245). They concluded that the treatment seemed definitely to reduce the average duration of fever and illness in patients who recovered, and it appeared to decrease the liability to empyema amongst the survivors. They recommended that each case be typed as soon as possible, and that where this could not be done at once a preliminary dose of 20,000 units of Type I and II sera together should be given, followed later by the specific type serum, treatment being continued by injection of 20,000 units at a time, twice a day, with approximately an 8-hour interval, an average total of 80,000 units being required.

In America, antipneumococcic sera, prepared according to Felton's method, are now used almost to the exclusion of the unrefined sera. *New and Non-Official Remedies* (1940) describes Anti-Pneumococcus Serum (Refined and Concentrated) Type I, Type II, Types I and II combined, Types IV and VIII combined, Types V and VII combined, and Type VII. The sera are also coming into general use in this country and several Types are now available commercially.

**Anti-Pneumococcus Sera (Refined and Concentrated)** of various Types and dosages are issued by *Parke, Davis & Co., London*; *Burroughs Wellcome & Co., London*; and *Lederle Laboratories, New York* (C. F. Thackray, Leeds).

**Rabbit Anti-Pneumococcus Serum.** Recently a serum has been developed derived from rabbits. It has been shown that rabbits form antibodies to the pneumococcus more rapidly and in greater amount than do horses, and owing to the fact that the globulin molecule in the rabbit is only one quarter the size of that in the horse, it is thought to pass more readily through vascular endothelium and to have greater diffusibility. Although encouraging results have been reported (especially from Denmark, where it has been widely used), sufficient time has not yet elapsed for a final evaluation.

The production of antipneumococcus rabbit serum.—B. S. Fritz, *Amer. J. Publ. Hlth*, 1939, 29, 224.

Description of rapid method for producing diagnostic type-specific antipneumococcic sera in rabbits, and methods of determining potency and specificity.—Welch, Borman and Mickle, *Amer. J. Publ. Hlth*, 1939, 29, 35 and 43.

69 patients with lobar pneumonia caused by pneumococci of Types I, II, V, VII, VIII, and XIV were treated with homologous rabbit antipneumococcus serum. None of the patients died when treated within the first ninety hours of the disease, and the mortality rate for the entire series was 7.4%. There were no severe untoward reactions and the incidence of serum sickness was lower with rabbit serum than with horse serum. None of the patients were found to be sensitive to rabbit serum. The minimum quantity of serum, measured in Felton units, which has been found adequate to treat lobar pneumonia is considered as the projected or necessary dose. The projected dose was given in one

administration in the 69 cases, and was found to be sufficient in 40. As much as 500,000 units, included in a volume of 500 ml. of unconcentrated and refined rabbit antipneumococcus serum, has been given in one administration without any untoward effects. From 10 to 15 grains of aspirin is given by mouth just prior to the administration of the serum.—E. H. Loughlin *et al.*, *J. Amer. med. Ass.*, ii/1938, 497.

Intramuscular injection of sera into human patients not suffering with pneumonia showed that the pneumococcus antibody Type I was absorbed more rapidly, and reached and maintained a higher titre than the same antibody in horse serum.—Finland and Brown, *J. Immunol.*, 1938, 36, 245.

Forty-five cases of pneumococcal pneumonia were treated with homologous type-specific immune rabbit serum. In 36 cases early recovery by crisis or rapid lysis ensued—no serious serum reactions occurred and there were only 2 deaths in this series.—V. B. Calloman, *Amer. J. med. Sci.*, 1939, 198, 349.

Data collected in Copenhagen hospitals between 1936 and 1938 show that if adequate serum therapy is given within the first four days of the disease, the mortality in lobar pneumonia is reduced to less than 10%. Rabbit serum is just as effective as horse serum.—N. I. Nissen, *Acta. Med. Scand.*, 1939, 98, 231.

The pneumococcal rabbit serum issued by the State Serum Institute, and now in general use in Denmark, has been found to be quite as effective as horse serum and only about one-tenth as expensive. The concentration of the serum has been increased so that now there are 4000 to 6000 units in every ml. The serum is usually given intravenously.—per *Lancet*, ii/1939, 449.

**Serotherapy and Chemotherapy.** The important advances made during the past decade in the typing of the pneumococci, and in the preparation and clinical use of type-specific sera, have recently been somewhat overshadowed by the outstanding achievements of chemotherapy, and in particular of sulphapyridine, in the treatment of pneumonia. In view of the obvious advantages and conveniences of chemotherapeutic agents, combined with their undoubted efficacy, there is a possibility that they may entirely supplant serum therapy. At the same time, as has been pointed out by Fleming and others, different strains of pneumococci vary enormously in their sensitivity to sulphapyridine, and where it is not possible to test the sensitivity of the infecting organism to the drug, a good case may be made out for the simultaneous use of vaccines or serums in order to increase the patient's immunity and improve his chances of recovery.

*For references to the use of chemotherapy in pneumonia see pp. 964, 970, and for further information concerning the bacteriology of pneumonia see Vol. II.*

### **Rheumatoid Arthritis.**

**Streptococcus Rheumaticus Vaccine.** *Syn.* ANTIRHEUMATIC VACCINE.

Prepared from killed cultures of streptococci isolated from rheumatic cases.

**Dose.**—Initial dose 1 to 5 millions. Subsequently at weekly intervals, with a 50% increase each time.

Extreme caution in the use of this vaccine is necessary. Even 500,000 may cause a most unpleasant reaction, and until the urine is free from organisms more than 5 millions can seldom be given.

Although they have been employed for many years, opinion is still divided as to the value of vaccines in rheumatoid arthritis, and they no longer enjoy any widespread use. It would appear



to be a matter of personal opinion whether a stock vaccine or an autogenous vaccine should be employed, but it is generally agreed that whichever is used it should be given over a prolonged period, in small doses, and with a careful avoidance of reactions. Vaccines should never be used in acute rheumatism, and should preferably be given subcutaneously. The initial dose should be small; 1 million organisms is usually sufficient and injections are given at weekly intervals. Even a mild reaction is sufficient to indicate that the dose should not be increased at the next injection. The injections are continued so long as improvement is occurring, but if there is no benefit within two or three months they should be stopped. Physiotherapy should be avoided during the period of vaccine treatment.

It has been suggested that any improvement following the use of these vaccines is due to non-specific desensitisation, and in view of the successful results attending the use of *B. coli* vaccines, T.A.B. vaccines, etc., in rheumatoid arthritis there would appear to be some foundation for this view.

A questionnaire sent to all patients treated during the year 1928-9 at the Devonshire Hospital, Buxton, showed that there was no evidence of greater benefit in those treated with autogenous vaccines than in the vaccine group as a whole, and it would appear that vaccines show no better prospect of improvement or cure of infective arthritis than other methods of treatment.—P. M. Congdon, *Lancet*, i/1932, 180.

The use of vaccines in rheumatism rests on pure empiricism. It is justifiable to employ them in selected cases under close observation, with the object of obtaining more precise information, but their routine use, with any implication of certain cure, cannot be too strongly deprecated.—E. P. Jordan, *J. Amer. med. Ass.*, ii/1937, 1444.

Results with vaccine in juvenile rheumatism have been inconclusive. Haemolytic streptococcus vaccine given intravenously in 47 rheumatic children with negative results.—W. Sheldon, *Lancet*, i/1938, 769.

122 patients with chronic arthritis were observed for from 6 months to 4 years; treatment consisted of weekly subcutaneous injections of 0.5 ml. of saline solution in 97 cases, and intravenous injections of polyvalent streptococcus vaccine in 25. Of 64 patients with chronic osteoarthritis treated by saline, 56 were improved. Of 58 patients with chronic rheumatoid arthritis, 33 treated with saline injections were improved (72%), and of 25 treated with vaccine, 17 were improved (68%). The psychological effect of the injection itself, rather than the substance injected, seems important, and this factor, plus the tendency to natural remission, may explain the high percentage of improvement.—N. Sidel and M. I. Abrams, *J. Amer. med. Ass.*, i/1940, 1740.

Treatment with *formolised bacterial filtrates*, based on the premise that chronic non-specific infectious arthritis presents a problem of re-infection of a previously sensitised host. It was thought that if these patients could be treated by the same substances to which they are allergic there might result an antigenic stimulation of some value. Strains of streptococci were isolated from patients with active rheumatoid arthritis and cultures made from teeth, tonsils, throat, nasopharynx, nose, sinus puncture, urine and stool. These were grown in beef-heart broth with a pH of 7.7 to 7.8. Only the strains having potent soluble toxins were used. The filtrates were then treated with formalin, the same as in diphtheria toxoid. Dilutions were then made of 1:10, 1:100, 1:1000, 1:10,000. Treatment by subcutaneous injection was begun with 0.1 ml. of the highest dilution, and increased gradually according to the patients reaction to the original test dose of the toxin and the reaction to the therapeutic dose. Individual dosage is essential. A very slight local reaction at the site of injection was considered favourable and was used as a guide in raising the dosage. The intradermal tests were used as indicators of the type of streptococcus probably responsible, and the one giving the strongest reaction was used in treatment, but only in single strain.

Whenever possible autogenous material was used. Otherwise, treatment was given with stock strain giving the strongest reaction. Treatment was given twice a week and continued for 3 to 6 months or longer. Of 100 cases treated (in various stages of the disease) 43 showed marked improvement, 26 moderate improvement, and 31 were failures.—A. C. Gordon, *J. Lab. clin. Med.*, 1937, 22, 559.

**Rheumatic convalescent serum.** Preliminary observations on the use of convalescent serum in the treatment of acute rheumatism. The serum was taken from patients in good general condition, free from cardiac complications and with a sedimentation rate approaching normal, about the fourth to eighth week after the temperature had settled. The serum was given intramuscularly or intravenously in doses of 10 to 20 ml. Of 15 cases treated, 9 were considered to have benefited. When given in the early stages of an attack the serum appeared to reduce the period of pyrexia, especially in primary attacks, and arthritic pain was relieved in such cases. Partial collapse appeared in two cases shortly after receiving an injection of the serum.—C. A. Green *et al.*, *Proc. R. Soc. Med.*, 1940, 33, 275; see also *Brit. med. J.*, ii/1939, 1291.

**Lipovaccine (Research Products, London).** An oily suspension of polyvalent streptococci, containing 5 million organisms per ml. with the addition of Gomenol 2% as antiseptic. For the treatment of fibrositis, except when associated with rheumatoid arthritis. *Dose.*—Initially, 5 ml. by deep injection into the fibrositic area, the needle being moved from place to place to secure even distribution. Subsequently the dose is increased up to as much as 40 ml., the injections being given at intervals of 5 to 7 days.

**Scarlet Fever.** Scarlet fever is an infection due to certain strains of *S. hæmolyticus*, the rash and the constitutional symptoms being due to absorption of the toxin.

**Antitoxinum Scarlatinum (B.P.C.).** *Syn.* STREPTOCOCCUS ANTITOXIN (SCARLATINA), SCARLET FEVER STREPTOCOCCUS ANTITOXIN CONCENTRATED (GLOBULIN).

An antitoxin prepared from the serum of horses that have been immunised by injection of the toxic culture filtrates of *Streptococcus hæmolyticus scarlatinae*, or of the toxin from this organism, or by a modification of these methods. There is no international unit for this antitoxin. The potency is sometimes stated in terms of a "unit" based on a skin test on the human subject. The test (which is an application of the Dick Test, *q.v.*) depends upon the fact that injection of the toxin intradermally produces in non-immune subjects a reddening of the skin; if the toxin is mixed with antitoxin before injection this reaction does not occur. The original neutralising unit of the Dicks was the amount of antitoxin required to neutralise one skin dose of toxin. The United States Public Health Service has adopted a "unit" (the American unit) which is the amount of antitoxin capable of neutralising 50 skin-test doses of toxin, *i.e.*, it is 50 times the original neutralising unit of the Dicks. Another method of assay (used in Great Britain) is the Parish-Okell rabbit method. 0.25 ml. of a satisfactory antitoxin injected into the vein of a rabbit will protect it against the subsequent injection of 6 ml. of a virulent culture containing the *Streptococcus scarlatinae*. The manufacture of the antitoxin is controlled by patent.

The absence of agreement regarding a satisfactory "unit" has led to lack of uniformity in statements of dosage; this is variously stated in terms of volume and of the (American) "units" described above, without any direct correlation.

*Dose for Treatment.*—10 to 30 ml. (equal to about 3000 to 9000 U.S.A. units) according to severity of case.

*Dose for Prophylaxis.*—5 to 10 ml. (1500 to 3000 U.S.A. units) for children of 5 to 15 may confer passive immunity for 10 to 14 days.

*Uses.* Serum therapy now plays an important role in the treatment of severe forms of scarlet fever. Early administration rapidly alleviates the toxæmic symptoms, arrests the progress of complications and may lessen the severity of complications already developed. It is best given intramuscularly, but in severe attacks intravenous injections are preferable. From 10 to 30 ml. of serum is adequate for the treatment of a simple case of scarlet fever, but toxic or severe cases may require from 60 to 120 ml. It need not be administered in mild attacks except in weakly children.

The serum may also be employed for the production of passive immunisation, from 5 to 10 ml. intramuscularly, producing immunity in a few hours which will last for 10 to 14 days, but there is little to recommend its use in general practice.

In addition to its use in scarlet fever it has also been used in the treatment of other acute streptococcal infections, especially puerperal septicæmia and acute rheumatism.

*Schultz-Charlton Reaction.* This is a diagnostic test to distinguish the rash of scarlet fever from other rashes. 0·2 ml. of streptococcus antitoxin (scarlatina) is injected intradermally into the chest, abdomen or forearm, where a uniform scarlet-fever rash not more than 70 hours old is available. A blanching 10 mm. to 40 mm. in diameter appears 4 to 10 hours later, and persists from 12 to 72 hours in most patients suffering from scarlet fever. The antitoxin may be used undiluted or diluted 1 in 10 in normal saline solution—diluted antitoxin should not be used later than six months after preparation.

Intravenous antitoxin in scarlet fever. 10 to 20 ml. dose in acute stage stops the acute process in a few hours.—H. S. Banks and J. C. H. Mackenzie, *Lancet*, i/1929, 381; H. S. Banks, *Lancet*, i/1929, 1248.

As regards the use of scarlet-fever antitoxin, most observers probably are now agreed that an early and sufficient dose aborts the initial toxæmia and thus puts some check on subsequent complications, though the evidence as to the value of serum in averting complications is somewhat conflicting. In Rumania, convalescent human serum has been used with considerable success.—J. V. Armstrong, *Lancet*, ii/1939, 327.

The administration of anti-scarlatinal serum advocated in every case; great prophylactic value in the prevention of otitis media.—S. Sutherland, *Lancet*, ii/1939, 328.

*Passive Immunisation.* A new scarlet fever antitoxin has been tested as a means of passive prophylaxis in the wards of the Gt. Ormond St. Hospital for Sick Children. The sera employed (Lederle Laboratories) are refined and concentrated and are said to contain the pseudoglobulin fraction only. The dosage recommended by the makers for passive protection against scarlet fever is 1 to 1·5 ml., but a routine dosage of 0·75 ml. was employed. Secondary cases were practically abolished in the hospital during the year in which it was used. In prophylactic doses it gave rise to serum reactions in less than 2% of cases.—D. B. Bradshaw, *Lancet*, ii/1939, 6.

**PUERPERAL SEPTICÆMIA.** Scarlatina antitoxic serum used in puerperal septicæmia with mortality 29·6%. In every case *S. pyogenes hæmolyticus* was found.—H. Burt-White, *Lancet*, i/1930, 19.

There is no trustworthy clinical evidence that the administration of anti-streptococcal serum for the treatment of human infections by hæmolytic streptococci has had any specific curative effect. The evidence obtained in puerperal fever cases at Queen Charlotte's Hospital suggests that such administration may sometimes have an *unfavourable* effect on puerperal infections by hæmolytic streptococci, and in such cases it is best not to interfere with the immunising mechanism of the patient until we can be sure that such interference does not do harm. Until our knowledge of the immunisation against hæmolytic streptococci has progressed further it would seem desirable to discontinue the use of antistreptococcal sera in the treatment (and prophylaxis) of puerperal fever and "surgical sepsis."—L. Colebrook, *Lancet*, i/1935, 1085.

**RHEUMATIC POLYARTHRITIS (ACUTE).** In a series of 44 cases, concentrated antiscarlatinal serum has proved itself an effective form of therapy worthy of extended trial. Patients were previously tested for serum sensitivity by intradermal injection of 0.2 ml. of a 1 in 10 dilution of serum. Non-sensitive patients received 30 ml. of serum intramuscularly and this dose repeated in 36 hours. This dose is equivalent to 18,000 new units of antitoxin (New York State Board) or to 900,000 old Dick units. Sensitive patients are desensitised as follows: give 0.2 ml. subcutaneously as the initial dose and double this each half hour until 2 ml. has been given; the remainder of the 30 ml. is given as 8 ml. and 20 ml. intramuscularly at half-hour intervals. Serum therapy is of value in the treatment of patients resistant to salicylates. The incidence of relapses is considerably lower with serum than with salicylates, and the stay in hospital and duration and nature of the convalescence compare very favourably with the latter. It is safe to give serum to very ill patients, even when suffering from grave carditis. The disadvantages attached to its use are that the average initial period of fever is longer, and there is a certain amount of discomfort from serum sickness.—J. Eason and G. Carpenter, *Quart. J. Med.*, 1937, 93.

**Serotherapy and Chemotherapy.** There has so far been no evidence to suggest that the sulphonamide derivatives are more effective than serum in the treatment of scarlet fever, but they are of undoubted value in dealing with complications such as otitis media, and in septic attacks they may usefully be employed to supplement serum therapy.

The results with sulphanilamide in a dose of 2 to 6 g. daily in 200 cases were distinctly inferior to those in a parallel series of serum-treated cases. The initial toxæmia was uninfluenced by the drug, and heavy desquamation was common. H. S. Banks, *Lancet*, ii/1939, 328.

For mild cases treated at home, no antitoxin or sulphanilamide; for mild cases admitted to an open ward, antitoxin intramuscularly; for all moderate cases antitoxin intramuscularly; for severe cases, antitoxin intravenously; for complications, sulphanilamide.—M. Mitman, *Lancet*, ii/1938, 329.

**Toxinum Scarlatinum (B.P.C.).** *Syn.* STREPTOCOCCUS TOXIN (SCARLATINA), SCARLET-FEVER STREPTOCOCCUS TOXIN.

The diffusible exotoxin obtained from a broth culture of a good toxin-producing strain of *Streptococcus hæmolyticus scarlatinae*. The organism is grown in a suitable fluid medium which is then centrifuged and filtered through a bacteria-proof filter. The potency of the toxin is expressed in skin-test doses (S.T.D.). One S.T.D. is the amount required to give, on hypodermic injection, an erythematous zone 10 mm. or more in diameter in the majority of susceptible persons.

The toxin, suitably diluted, is used in the Dick Test for susceptibility to scarlet fever, and also for actively immunising those who are susceptible, though during the present mild phase of scarlet fever it is not advisable for general application.

**Dick Test.** The toxin is diluted with normal saline so that 1 S.T.D. is contained in 0.1 to 0.2 ml., and this quantity of toxin is injected *intradermally* (not subcutaneously) into the front of the forearm, the site having been carefully cleansed. If the patient is susceptible to scarlet fever, a positive reaction will appear, reaching a maximum in 18 to 24 hours and characterised by a circumscribed area of redness, about 1 to 2 cm. in diameter, which persists for a few days and then fades, leaving a brownish pigmentation. The slightest reddening constitutes a positive reaction provided it attains a diameter of 10 mm. Owing to the high dilution of the toxin, pseudo reactions are very rare and a control is unnecessary. The syringe and needle must *not* be sterilised by means of alcohol since this precipitates the toxin; they should be boiled in distilled water.

**Active Immunisation.** Streptococcus toxin (scarlatina) produces a more permanent immunity than that conferred by scarlet-fever antitoxin. It is administered subcutaneously or, preferably, intramuscularly. Five injections should be made at 5 to 7-day intervals, the doses being 500, 2000, 8000, 25,000 and 80,000 skin-test doses respectively. In strongly Dick-positive reactors the initial dose may be reduced to 250 S.T.D. In about 10% of cases a reaction occurs, characterised by vomiting, malaise and a scarlatiniform rash. The reaction may occur at any stage of the course. According to the Dicks, the reaction is prevented by administering 2 to 3 m. of 1 in 1000 adrenaline solution simultaneously with the toxin.

Local antitoxic immunity to scarlet fever toxin may be produced by intradermal injections of varying amounts of scarlet fever toxin. Repeated tests on the same person for scarlet fever immunity should not be made on the site of a previous test.—Dick and Dick, *J. infect. Dis.*, 1938, 62, 83.

### Septicæmia.

The term "septicæmia" is applied to conditions in which pathogenic organisms multiply in the blood, and give rise to symptoms of general poisoning, the commonest organisms found being streptococci and staphylococci, which gain entrance through abrasions in the skin or through the tonsils, nasal sinuses or the puerperal uterus.

**Serum Antistreptococcicum (B.P.C.).** The serum of horses that have been immunised by injections of streptococci. In the preparation of polyvalent sera, a large number of strains (hæmolytic, non-hæmolytic and *S. faecalis*) are used. They are obtained from a number of infections, *e.g.*, erysipelas, septicæmia, endocarditis, uterine infections, influenza, appendicitis, etc. Some strains of streptococci, *e.g.*, those from scarlet fever, erysipelas and puerperal sepsis, produce toxic culture-filtrates; injection into horses of these toxic products, as well as of the bacterial cultures, yields a serum that is antitoxic as well as antibacterial. The serum may be used without further treatment (natural serum), or the antibodies may be partially purified and redissolved in saline (concentrated serum).

**Dose.**—From 10 to 30 ml. intramuscularly, or intravenously when diluted with twice the volume of normal saline, and repeated daily or even 12-hourly for about a week. Early administration and adequate dosage is important.

The serum is employed in the treatment of general septicæmia, infective endocarditis, wound infections, etc., also in erysipelas, scarlet fever and puerperal fever, though in these latter conditions sera prepared from the specific strain of streptococcus are preferable.

Although the use of the sulphonamide derivatives has met with considerable success in the treatment of septicæmic conditions, better results may often be obtained by employing them in conjunction with serum therapy.

Antistreptococcic serum 50 to 70 ml. during labour, or a few days prior to onset, if trouble anticipated.—S. J. Cameron and H. Thomson, *Brit. med. J.*, i/1931, 350.

Streptococcic septicæmia treated with scarlet fever antitoxic serum. Given subcutaneously or intramuscularly, and never more than 20 ml. at a time.—A. B. Rosher, *Lancet*, i/1930, 129.

**ERYSIPELAS.** An antitoxin prepared by immunising horses with several strains (eight) of the streptococcus of erysipelas, used in 3311 cases over a period of five years at the Bellevue Hospital, New York, reduced the number of deaths by 30% and reduced the average duration of the disease by 60%, but only of value in controlling the immediate process, and does not prevent additional attacks. It is given intramuscularly in 10 ml. doses, commenced as soon as diagnosis is made, and repeated every 12 to 24 hours for 6 doses, when it is discontinued if no improvement is evident.—D. Symmers and K. M. Lewis, *J. Amer. med. Ass.*, ii/1932, 1082.

**Streptococcus Vaccine (Polyvalent).** Polyvalent vaccines are prepared from numerous strains of streptococci for use in localised infections, such as erysipelas, lymphangitis, ulcers, sinuses, tonsillitis, adenitis and mastitis; also in asthma and bronchitis, and in generalised infections such as septicæmia and pyæmia, provided the streptococcus has been proved to be responsible. *Initial dose* in very acute and in generalised infections should be 5 or at the most 10 millions; in more chronic conditions a dose of 25 to 50 millions is suitable and may be increased to 100 millions. The action of these vaccines is very erratic, however, and their value is doubtful. In erysipelas doses of  $\frac{1}{2}$  to 1 million may be repeated at intervals of 1 or 2 days. In most other conditions the interval between doses should be 6 or 7 days.

**FIBROSITIS.** In 25 cases of long standing the local injection of a lipovaccine was found of value. The lipovaccine was made up in two strengths, representing one and ten million organisms (polyvalent streptococci isolated from rheumatic cases) suspended in sterile olive oil. The oil was injected deeply into the fibrositic area and distributed throughout it by moving the needle; as much as 10 ml. of the stronger concentration used at one sitting. Within a few hours the area became hot and tender, with malaise and evening pyrexia, but all symptoms subsided at the end of a few days, leaving the fibrositic area comparatively painless and a marked gain in general health.—G. Laughton Scott, *Brit. med. J.*, i/1936, 302.

**Coley's Fluid.** Contains the combined toxins of *Streptococcus erysipelas* and *B. prodigiosus*, and has been employed in the treatment of inoperable cancer (especially sarcoma) and Hodgkin's disease.

**Dose.**—Inject a dose daily into tumour, or neighbourhood of tumour, beginning with 0.25 minim into the tumour, or 0.5 minim elsewhere, and if little or no

reaction increase by 0.25 or 0.5 minim daily till a rise of temperature to 102° to 104°F. is reached. For first few doses dilute with boiled water to ensure accurate dosage. If depression follows injections give at longer intervals. Continue injections till reaction has calmed down and temperature fallen.

### Snake Bite.

The chief poisonous snakes belong to the Colubrine and Viperine families. The former includes the cobras, coralline snakes, kraits, hamadryad and the death-adder, the latter includes the rattlesnake, puff-adder, bush-master and copperhead. A serum produced from a Colubrine venom is not effective against the venom of a Viperine snake and *vice versa*. Specificity is also shown by the antitoxins produced from the venoms of individual members of the two families.

**Serum Antivenenosum (B.P.C.), syn. ANTIVENENE**, is a generic name for anti-venom sera. It consists of the serum of horses immunised by subcutaneous injections of snake venom. The most useful serum for general use is prepared by injecting a mixture of 80% cobra venom and 20% viperine venom.

*Dose.*—100 ml. or more intravenously.

### Therapeutic Use of Snake Venoms.

During recent years snake venoms have been introduced into medicine for the treatment of numerous conditions, the venoms from different species of snakes being employed for different therapeutic purposes. Thus, cobra venom has been used as an analgesic in severe intractable pain, particularly in cancer, and this and puff-adder venom have also been employed in epilepsy. Moccasin venom is used in certain hæmorrhagic conditions, such as functional uterine bleeding and purpura hæmorrhagica. All of these are given by injection. Russell's viper venom and the venom of *Bothrops atrox* (fer-de-lance) are employed in dilute solution as local hæmostatics, and the former in particular is stated to be one of the most effective local hæmostatics available.

### Cobra Venom.

*Dose.*—The initial dose is usually 0.1 mg. of the dried venom, subcutaneously or intramuscularly, increasing up to 6 mg. Alternatively, the amount to be injected may be calculated in "mouse units," one unit being sufficient to kill a mouse of 25 g.

It has been employed with some success in the relief of pain due to carcinoma, trigeminal neuralgia, tabes, etc., especially when morphine is contraindicated or is losing its effect. It has also been used in epilepsy.

Although analgesia undoubtedly occurs, it is erratic and unreliable, and at its best is no better than that obtained with morphia. Trial in 51 cases.—J. Lavedan, per *Med. Annu.*, 1937, 419.

Of 14 cases of trigeminal neuralgia treated by cobra venom, 6 were cured and 4 improved. The initial dose was gradually increased to 4 mouse units, one intracutaneous injection being given every third day.—M. Brünner-Ornstein per *Brit. med. J., Epit.*, i/1937, 50.

Cobra venom relieves pain not through a peripheral action on sensory nerve endings or ascending nerve tracts, but through its effect on the central nervous system, more particularly the brain. The analgesic action on the brain, however, is not identical with that produced by morphine, for which it may sometimes be substituted clinically, because the higher or intellectual faculties are not depressed by cobra venom as they are by opium alkaloids. The *modus operandi* for cobra venom would therefore seem to be an action on some lower synapses, probably in the optical thalamus. Cobra venom seems to be less depressant for neuromuscular performance than morphine and other opiates. Unlike both narcotics and antipyretics it actually widens the field of vision. In contrast to opium alkaloids and other analgesics it actually stimulates intellectual performance. In moderate doses, e.g., 5 to 10 mouse units intramuscularly, it does not injure either the circulation or the kidney or liver functions. It has a wide margin of safety. It has been found a useful analgesic not only in patients with advanced cancer, but also in certain cases of chronic arthritis, neuritis and neuralgia (particularly tic douloureux), tabetic crises, and advanced Parkinson's disease. Of 115 cases treated, 65% experienced relief of pain.—D. I. Macht, *Med. Pr.*, i/1939, 254.

Of 17 cases suffering from severe intractable pain (carcinoma, ureteral spasm, interstitial cystitis), 46% were completely relieved and 88% were relieved of half their pain or more by injections of cobra venom, beginning with 2 or 3 ml (10 or 15 mouse units), and continuing the dosage at that level for 4 to 6 days, then lowering the dose to a maintenance level (usually 1 ml. = 5 mouse units). Injections must be given intramuscularly; subcutaneous injections cause redness and tenderness.—R. N. Rutherford, *New Engl. J. Med.*, ii/1939, 408.

The Council on Pharmacy and Chemistry of the A.M.A. considers purified cobra venom to be of some value for the relief of pain, especially that of inoperable cancer; it does not displace morphine completely in more than relatively few cases, but it is of value; it appears to be of limited value in the treatment of tic douloureux and the various conditions grouped under the names of rheumatism and arthritis; its therapeutic effects are variable and uncertain in all painful conditions; the disagreeable side actions, including nausea, vomiting, diarrhoea and pain of injection must be brought to the notice of those who use cobra venom; it must not be recommended for those who are severely ill, except those suffering from inoperable malignant tumours or from incurable disease. The effects are not immediate but may take hours to appear.—*J. Amer. med. Ass.*, ii/1940, 1196.

17 patients with intractable pain, principally from carcinoma of the cervix, treated with cobra venom, 5 mouse doses every other day; results good in 8, fair in 6, and poor in 3.—W. T. Black, per *Trop. Dis. Bull.*, 1940, 515.

Of 85 patients suffering from neuritis, sciatica and arthritis, 23 experienced marked relief, 23 definite relief, and 9 slight relief from intramuscular injections of cobra venom, given twice or thrice weekly in doses ranging from 1 to 20 mouse units.—R. N. Chopra and J. S. Chowhan, *Indian med. Gaz.*, 1940, 69.

### Puff-Adder Venom.

**Dose.**—The initial dose is 0.2 mg. of the dried venom subcutaneously, gradually increased to 10 to 12 mg. Solutions for injection should be freshly prepared.

This has been employed in the treatment of epilepsy. In a series of 14 cases treated in this country by B. Barnett (*Med. Annu.*, 1937, 418), 4 showed a complete cessation of fits, 1 was unaffected, and 9 were improved.

There is sufficient evidence of the successful treatment of epilepsy with snake venom to warrant further investigation. The treatment would, of course, be quite empirical, though reports seem to show it depends on something in the nature of protein shock.—B. Barnett (Curator of Reptiles, Zoological Society of London), *Brit. med. J.*, ii/1934, 1073. Dr. Burgess Barnett is prepared to advise medical men as to the most suitable form of snake venom for use in any particular type of case, and as to the method of obtaining an aseptic product by appropriate treatment of the venom.—R. H. Elliott, *ibid.*

**Venene**, prepared by F. W. FitzSimons from puff-adder venom, wight-adder venom, cobra venom and mamba venom, at the Port Elizabeth Museum and Snake Park (S. Africa), has been similarly used in epilepsy.



**Dose.**—Initially, for a healthy adult, 5 minims subcutaneously, increased at weekly intervals of 2, 3 and 4 weeks up to a maximum of 40 minims.

The preparation has been widely used for epilepsy in South Africa, and Mr. FitzSimons, in a paper read before a combined meeting of the British and South African Associations for the Advancement of Science, in July, 1929, reported encouraging results. There seems to be a *prima-facie* case for investigation of the claims. The benefits claimed may be due to desensitisation.—*Lancet*, ii/1930, 915.

### Moccasin Venom.

**Dose.**—The initial injection in patients over 10 years of age is 0.4 ml. of a 1 in 3000 dilution of the venom subcutaneously, rapidly increased to 1 ml., the injections being given twice weekly and continued for 2 or 3 months if necessary. For younger children the maximum dose is 0.6 ml.

This venom has been used in various hæmorrhagic conditions, such as intractable uterine bleeding, recurrent nasal hæmorrhage, symptomatic purpura, and purpura hæmorrhagica—but not hæmophilia.

**HÆMORRHAGE.** Moccasin snake venom given intradermally or subcutaneously has a definite effect in decreasing the permeability of the capillaries, and is of value in hæmorrhagic states other than hæmophilia or idiopathic thrombocytopenic purpura.—S. M. Peck and N. Rosenthal, *J. Amer. med. Ass.*, i/1935, 1066.

**MENORRHAGIA.** 7 cases of menorrhagia, in which no organic lesion could be demonstrated, were successfully treated by subcutaneous injections of a 1 in 3000 solution of moccasin venom. Initial dose 0.4 ml., increased by 0.2 ml. at 3-day intervals for the next two doses, when reaction usually occurred and the dose was reduced to 0.05 ml. Subsequent injections at 3-day intervals were increased to 0.1 ml. and then 0.2 ml., provided no untoward local reaction occurred. Dose then increased by 0.3 ml. until a dose of 1 ml. could be given twice a week. Injections continued for several months, but improvement usually within 1 or 2 months.—C. H. Watkins, *Proc. Mayo Clin.*, 1936, 261. See also Venoms and Antivenenes, a collection of abstracts from recent papers.—*Trop. Dis. Bull.*, 1936, 379.

**PURPURA HÆMORRHAGICA.** An intradermal moccasin snake venom test has been used as a prognostic measure in essential thrombocytopenic purpura hæmorrhagica. Persistence of a positive reaction to successive tests, or a reversal to a negative reaction, is of value in determining the trend of the purpuric state. Subcutaneous injections of moccasin snake venom have been employed as a therapeutic measure in chronic purpura hæmorrhagica. It apparently has been of value in 22 of the 34 cases in which it has been used. The effect of subcutaneous venom injections and the trend of the intracutaneous venom test are important for the indication and prognosis of splenectomy.—S. M. Peck, M. Rosenthal and L. A. Erf, *J. Amer. med. Ass.*, i/1936, 1791.

**EPILEPSY.** Eight institutional epileptics were treated for nine weeks with moccasin venom. Injections of a 1 : 3000 venom solution were used, beginning with 0.2 ml. and increasing by 0.2 ml. to a dose of 1 ml. Injections were given twice weekly till the maximum dose was reached, and then at weekly intervals. The frequency and severity of the seizures were compared during the period of no treatment, during Luminal therapy and during venom therapy. During the administration of venom the frequency and severity of the seizures were greater than during the other periods and the patients were more irritable. It is concluded that venom therapy not only does not induce a refractory state to convulsive seizures in epileptics, but may render them more susceptible to seizures. There is no distinguishable difference in the physiological action of the venom of the water moccasin from that of the rattlesnake.—I. Finkelman, *J. Lab. clin. Med.*, 1937, 22, 572.

### Viper Venom.

The venom of Russell's viper is an effective local hæmostatic, both for cases of hæmorrhage due to superficial injuries and for

external wounds suffered by hæmophiliacs. The solution of venom is applied directly to the bleeding point by means of a pledget of cotton wool, or by dropping from a fine needle. It is especially valuable in dental surgery and following tonsillectomy. It may also be employed for the estimation of prothrombin (see H. W. Fullerton, *Lancet*, ii/1940, 195).

Snake venoms lose their toxicity before they are absorbed by the intestinal mucous membrane, so that in regard to the possibility of toxic effects, only that portion of the dose that comes in contact with the broken surface need be considered. If the susceptibility in man is the same as that in monkeys the estimated smallest fatal dose of Russell's viper venom is 42 mg.—B. Barnett and R. G. Macfarlane, *Brit. med. J.*, ii/1936, 1286.

**HÆMATEMESIS.** A severe case which had continued for more than 24 hours successfully treated by the oral administration of the contents of one phial of Stypven.—A. Barratt, *Brit. med. J.*, ii/1936, 1083.

**HÆMOPHILIA.** The venom of Russell's viper clots hæmophilic blood more quickly than any other venom—one drop of a 1 in 1000 solution added to 10 drops of hæmophilic blood causes clotting in 17 seconds, and a 1 in 100,000 solution in 60 seconds, the clot being tough and firm. The solution is easily sterilised by filtration through a Berkefeld filter: the venom maintains its potency unchanged when dry, but soon deteriorates in dilute solution. Striking results in local hæmorrhages (e.g., from tooth sockets) in hæmophiliacs; bleeding stopped at once by application of 1 in 100,000 solution.—R. G. Macfarlane and B. Barnett, *Lancet*, ii/1934, 985.

**Hæmorrhage in a hæmophilic boy successfully controlled by application of 1 : 10,000 dilution of Russell's viper venom.**—G. A. Baker and P. C. Gibson, *Lancet*, i/1936, 428.

**Snake venom and its use in dental hæmorrhage.**—J. Draper Cambrook, *Proc. R. Soc. Med.*, 1936, 281.

**Rusven (Boots, Nottingham).** Venom of Russell's viper for external local application in the treatment of hæmorrhage.

**Stypven (Burroughs Wellcome, London).** Russell's viper venom for topical application in the control of external bleeding. It is issued in rubber-stoppered bottles accompanied by hermetically sealed ampoules of solvent consisting of sterile distilled water containing 0.5% of phenol.

**Fer-de-Lance Venom Solution (Lederle Laboratories, New York; C. F. Thackray, Leeds).** A 1 in 5000 solution of the venom of *Bothrops atrox* (fer-de-lance) in 50% glycerin. For use as a local hæmostatic, especially in dental practice.

## Staphylococcal Infections.

**Antitoxinum Staphylococcicum (B.P. Add.1).** Prepared from the serum of horses that have been immunised by injections of the toxin of *Staphylococcus aureus*. It may consist either of the unconcentrated or of the concentrated (globulin) serum, either in the dried or liquid state.

**Dose.**—Prophylactic, 2000 to 4000 units. Curative, 10,000 to 20,000 units, intravenously or intramuscularly, repeated after 12 or 24 hours.

**Uses.** Although the majority of cases of staphylococcal infection of the skin respond to local treatment with or without treatment with vaccine or toxoid, in some patients a generalised toxæmia or septicæmia may follow. The antitoxin appears to be chiefly efficacious in pyæmic cases. Useful in acute staphylococcal infections and toxæmias so long as the cocci are not detectable in the circulating blood. Few cases of staphylococcal bactæmia recover, except when the primary focus is in the bone marrow;

treatment with staphylococcal antitoxin should supplement surgical measures, and will sometimes avert a fatal issue.

Prophylactically, it is employed when there is risk of a generalised infection, *e.g.*, from carbuncles, osteomyelitis and mastoiditis, or before operations.

A serum obtained by immunisation of horses, first with toxoid and afterwards with unaltered toxin, given intramuscularly in 104 cases of staphylococcal infection, ranging from carbuncle to septicaemia; as much as 800 ml. may be needed in a severe case. Of 64 patients in whom positive blood cultures were obtained, 29 recovered.—C. E. Dolman, *per Brit. med. J.*, ii/1934, 950.

**Vaccinum Staphylococcicum (B.P.C.).** *Staphylococcus vaccine* is prepared from killed cultures of *Staphylococcus albus*, *S. aureus* and *S. citreus* (mixed vaccine), or from *S. aureus*, or (less commonly) from *S. citreus* or *S. albus* alone.

**Dose.**—Initial, 100 millions, increased to 1000 or even 5000 millions, at intervals of 7 days.

**Used** in the treatment of localised staphylococcal infections, *e.g.*, furunculosis. Often an autogenous vaccine is to be preferred to a stock one.

In cases of acne, *Staphylococcus albus* is commonly associated with the acne bacillus (*q.v.*). In boils, carbuncles, sycosis, ulcers, and sinuses generally, and in acute generalised infections, such as pyaemia, ulcerative endocarditis, septicaemia and in peritonitis, either *S. albus* or *S. aureus* may be found, but *S. aureus* is relatively the more common. The mixed vaccine may, if necessary, be used.

**Propidex** (*Pharmaceutical Specialities (May & Baker) Ltd., London*). Antistaphylococcal ointment. A mixed vaccine of streptococci, staphylococci and *E. pyocyaneus*, for local application to surface lesions of a pyogenic nature—boils, carbuncles, etc.

**Staphar** (*Bayer Products, London*). Mixed staphylococcus vaccine. **Dose.**—0.5 to 0.75 ml. subcutaneously or intramuscularly, increasing to 1 ml. 3 times weekly. Staphylococcal infections.

**Staphylococcus Toxoid.** The staphylococcus toxin, like diphtheria toxin, can be converted to toxoid by formaldehyde. To a high-potency staphylococcus toxin, formaldehyde is added to give 0.1 to 0.15% *w/w* of HCHO and the mixture incubated at 37° for 14 days.

**Dose.**—0.05 ml., increased to 1.0 ml. at intervals of 7 days.

Staphylococcus toxoid may be used instead of the vaccine in the treatment of chronic staphylococcal infections. It is especially useful in severe cases, *e.g.*, recurrent furunculosis, chronic and sub-acute osteomyelitis and in patients convalescing from acute staphylococcal toxæmia.

**Report of the Therapeutic Trials Committee.** Amount of circulating antitoxin readily increased by injections of staphylococcus toxoid, and this is attended with clinical improvement in the majority of cases of furunculosis, but acne does not respond as well as do pure staphylococcal infections. Doses of 0.05, 0.1, 0.2, 0.3, 0.4 and 0.5 ml. at weekly intervals, intramuscularly. Very few reactions noted.—D. S. Murray, *Lancet*, i/1935, 303.

Of 23 cases of sycosis barbæ treated with injections of toxoid, 12 were cured and the remainder much improved. Of 24 cases of staphylococcal infection

other than sycosis (mostly carbuncles and boils) 18 were cured and the remainder much improved.—J. I. Connor, *Brit. med. J.*, ii/1935, 1195.

Favourable results, with no serious reactions, in treatment of staphylococcal infections of the skin with sterile formalinised filtrates of staphylococcus cultures.—M. A. Gohar, *J. trop. Med. (Hyg.)*, 1935, 259.

Alum precipitation increases potency of the toxoid.—Leonard and Holm, *J. Immunol.*, ii/1935, 209.

Method for the production of staphylococcus toxin and toxoid. Toxoid should contain at least 6 flocculating units per ml. and at least 5 antitoxin-binding units per ml.—Dolman and Kitching, *J. Path. Bact.*, 1935, 137.

Antigenic efficiency of staphylococcus toxoid should be maintained in respect of leucocidin as well as alpha-hæmolysin.—F. C. O. Valentine, *Lancet*, i/1936, 526.

Immunisation is a delicate process which if over-exercised may lead to diminished immunity, and as we immunise we may also hypersensitise, since immunity and hypersensitivity are not antagonistic but may co-exist. Thus, one must try to immunise as efficiently as possible and avoid sensitising; the most probable way to effect this is to give the shortest possible course of injections consistent with recovery. In a case of furunculosis the most successful method seems to be to begin treatment immediately a lesion has become definitely circumscribed or has opened; to begin with, a small dose of toxoid such as 0.1 ml. of 1 in 10 is given, rapidly increasing with bi-weekly injections up to 0.5 ml. of undiluted toxoid, avoiding severe local reactions. This can usually be done in three weeks. Then, if there are no fresh lesions, treatment is stopped. If a fresh boil begins to appear at any time in the next few weeks or months, a single small dose of toxoid is given at once, and it is remarkable how often these recurrent lesions abort.—P. N. Danton, *Proc. R. Soc. Med.*, 1936, 30, 516.

The results obtained by the use of the toxoid in a small series of cases (20 cases of sycosis and 13 cases of boils) were not sufficiently encouraging to justify a continued trial. The injection of staphylococcus toxoid constantly increased the circulating antihæmolysin. There was no evidence, however, that this increase had any clinical value. Toxoid has no evident advantage over the use of "non-specific" antigens or other treatments for multiple boils.—R. Klaber, *Lancet*, ii/1936, 786.

G. Ramon states that the efficacy of refined staphylococcus anatoxin in affections due to staphylococci, especially skin diseases such as furunculosis, onychia, sycosis, and acne, is proved by his study of more than 15,000 cases during the last three years. The first injection consists of 0.1 ml., the second of 0.25 ml., the third of 0.5 ml., the fourth of 1 ml., and subsequent injections of 2 ml., the doses being halved for children. The injections should be given subcutaneously at 4 or 5 day intervals. No serious reactions have been observed.—per *Med. Annu.*, 1940, 429.

**Staphylococcus Vaccine Toxoid (S.V.T.)** (*Lister Institute, London; Allen & Hanbury, London*). A mixture of staphylococcus vaccine and staphylococcus toxoid—1000 millions staphylococci and 0.5 ml. toxoid per ml. *Dose*.—0.1 ml., increased to 1 ml. at intervals of 4 to 7 days.

**Staphylococcus Vaccoid** (*St. Mary's Hospital, London; Parke, Davis, London*). A mixture of staphylococcus vaccine and toxoid; issued in two strengths, (a) for children, contains 60 millions of staphylococci per ml., with "weak" staphylococcus toxoid; and (b) for adults, contains 300 millions of staphylococci per ml. with "strong" staphylococcus toxoid. *Dose*.—0.1 ml., increased to 1.0 ml. at intervals of 7 days.

**Staphygen** (*Bayer Products, London*). A staphylococcus formol toxoid preparation. *Dose*.—0.1 ml., increasing to 1 ml. at 2 to 3 day intervals.

**Tetanus.** The tetanus bacillus is found in cultivated and manured soils and in the faeces of various animals, especially the horse. Infection usually occurs from wounds and minor injuries; punctured wounds, infected compound fractures, abrasions and lacerations into which dirt has been introduced are especially liable to cause tetanus. The incubation period is usually from eight to twelve days. The bacilli multiply in the wound and produce toxin

which is conveyed to the spinal cord by the motor nerves, and to the medulla and brain stem by the blood stream. If sufficient antitoxin is given in the early stages the central spread of toxin is checked and that which is in circulation is neutralised, so that tetanus either does not develop or appears only in a mild form, but once the symptoms have developed the outlook is more grave. Early diagnosis is therefore of great importance, among the first symptoms being an unexplained rise in temperature, abdominal rigidity, increased nervousness, temporary giddiness, violent headache, trembling of the tongue, profound sweating and slight stiffness of the neck and jaws.

### **Antitoxinum Tetanicum (B.P., U.S.P. XI).**

Prepared from the serum of horses that have been immunised by injections of the toxin or toxoid of *Bacillus tetani* (*Clostridium tetani*); the serum may be used in the liquid state or dried, or it may be concentrated by precipitating the antitoxin-containing globulins which are used either in solution or in the dry state. Liquid preparations for prophylactic use contain not less than 300 units per ml., and for therapeutic use not less than 1600 units per ml. Solid preparations contain not less than 3000 and 16,000 units per g. respectively. U.S.P. XI recognises only the solution of the antitoxic globulins and requires a potency of not less than 300 U.S.A. units (approximately 600 international units) per ml.

*Dose.*—Prophylactic, 1000 to 2000 units; therapeutic, 20,000 to 40,000 units.

(a) **Prophylactic Use.** An injection of 1000 to 3000 International Units within a few hours of receiving a wound soiled with dirt greatly reduces the probability of tetanus developing. The larger dose is strongly recommended by the Medical Research Council (*Brit. med. J.*, i/1939, 738) and doses up to 10,000 units may be used when the wound is not seen until the second day and shows signs of turning septic. The passive protection conferred lasts for about three weeks. During the war of 1914-1918 it was the rule among military surgeons to give a routine injection of 1000 International Units, preferably intramuscularly, as soon as possible after reception of a wound. Combined tetanus and gas gangrene antitoxins have also been employed prophylactically.

(b) **Use in Treatment.** Although the prognosis in an established case of tetanus is extremely grave, there is a wide measure of agreement that the use of antitoxin in large doses is of undoubted value. Opinions differ as to the best method of administration, but the combined administration of 40,000 International Units intrathecally (preferably by the cisterna magna), 20,000 to 40,000 units intravenously, and the same amount intramuscularly, is probably the most popular method, though some workers prefer to give a single massive dose of 100,000 or 200,000 units intravenously. An objection to the intrathecal injection is that it is

liable to set up an irritation and cause serous meningitis. It is important to note that treatment of the wound should not be undertaken until at least an hour after the antitoxin has been given. For the control of the spasms, bromides, chloral hydrate, morphine, or chloroform inhalations may be given simultaneously with the antitoxin; many workers now favour the rectal injection of brom-ethol or paraldehyde.

Better results obtained by giving large doses (50 to 100 ml.) subcutaneously by the intraspinal route *under chloroform anaesthesia*, ending with subarachnoid injection of 10 to 30 ml. The chloroform impregnates the lipoids of the nervous system, rendering it impossible for the toxins to become fixed—an example of "phylaxis."—René Cruchet, *Brit. med. J.*, i/1932, 86.

Toxin which has been absorbed by nervous tissue can be displaced by the vapour of a general anaesthetic, and can then be neutralised by antitoxin. Dufour's method consists in giving either chloroform or ether as a general anaesthetic, and administering antitoxin by any parenteral route, preferably by the intravenous drip method. The anaesthetic is given for half an hour twice a day, and two or three administrations may be sufficient.—C. T. Barry, *Brit. med. J.*, ii/1936, 896.

Five cases of tetanus treated with doses of from 160,000 to 200,000 units of antitoxin—sodium Luminal and Avertin used as sedatives. Avertin more efficacious in producing relaxation.—E. T. Freeman, *Brit. med. J.*, i/1936, 552.

Best treated by a combined method of administration of the antitoxin, intrathecally through the cisterna magna (40,000 units), intravenously and intramuscularly (80,000 units in equal parts), with daily administrations of 40,000 to 80,000 units, according to the severity of the case, intravenously or intramuscularly, or both, until spasms are fully controlled. The routine use of paraldehyde per rectum is recommended in all cases as the most suitable sedative. The total mortality in a series of 438 consecutive cases was 50.6% and 29.4% after excluding those that died within 24 hours of admission.—B. B. Yodh, *Brit. med. J.*, i/1937, 855.

The treatment of tetanus should aim at preventing the absorption of toxin by the central nervous system, controlling reflex spasms and maintaining strength. Antitoxin in doses of 200,000 units intravenously is recommended, together with Avertin.—L. Cole, *Proc. R. Soc. Med.*, 1938, 31, 1205.

There is usually unnecessary delay in making a diagnosis and therefore in giving antitoxin. The administration of antitoxin at the earliest possible moment is as important in tetanus as it is in diphtheria. Prophylactic antitoxin should be repeated in all cases of suspicious wounds, and all soldiers before going on active service should be actively immunised against tetanus. It is unnecessary to continue to give antitoxin when reflex convulsions have ceased, and only tonic rigidity remains, except when there is a septic wound which cannot be drained.—L. Cole, *Lancet*, i/1940, 164; see also *Brit. med. J.*, i/1940, 742.

### **Toxinum Tetanicum Detoxicatum (B.P. Add. II). Syn. TETANUS TOXOID, ANATOXIN.**

*Dose.*—0.5 to 1 ml. subcutaneously or intramuscularly.

Tetanus toxin, the toxicity of which has been removed by the action of chemical substances while retaining its immunising properties. It may occur either as (a) tetanus toxoid in simple solution, prepared by treating the filtrate with formaldehyde, or (b) as alum precipitated tetanus toxoid, prepared by adding alum to tetanus toxoid in simple solution, separating the precipitate and washing and suspending it in normal saline.

The injection is preferably made in the back of the left arm, a second injection being given after an interval of three months.

Tetanus toxoid, or alum-toxoid, is employed for the production of active immunity to tetanus in individuals (e.g., soldiers) who

are subjected to a greater than normal hazard of the disease. The injections are said to convey a lasting immunity.

Alum-precipitated tetanus toxoid in a dose of 1 ml. induces a higher degree of immunity than three doses of toxoid without alum.—D. H. Bergey, *J. infect. Dis.*, 1934, 55, 72.

Two injections of alum-precipitated toxoid better than three of unprecipitated toxoid.—Jones and Moss, *J. Immunol.*, i/1936, 115.

There seems to be no doubt that by the injection of toxoid, or of alum-toxoid which seems to give even better results, it is possible to confer complete and permanent immunity on the vast majority of those inoculated. The immunity thus produced results in a much greater and more active response to the antigenic stimulus, so that infection by tetanus bacilli at any later date will be countered by a rapid and increased output of antitoxin sufficient to afford complete protection. Such protection might be afforded to the British Army by the injection of two doses of alum-toxoid at an interval of three months, with the additional protection of a third inoculation before being called on for foreign service or in the event of war.—H. H. Brown, *Brit. med. J.*, i/1937, 494.

Because of the marked variation in individual response, and the lack of an easily performed test to determine immunity against tetanus, repeated injection of toxoid should be resorted to on the occurrence of an injury. Otherwise a false sense of security may result.—Herman Gold, *J. Amer. med. Ass.*, ii/1937, 481.

Anti-tetanus vaccination with tetanus anatoxin has received a unanimously favourable reception in France, where some one and a half million persons have been vaccinated. Compared with anti-tetanus serum the anatoxin was found to be stronger and more lasting. Serovaccination gives protection which is achieved rapidly, but is of short duration, and post-serum tetanus occurring as late as the third month after vaccination has been reported. Experience has proved that immunisation can become lasting if serovaccination and the use of anatoxin are associated as a routine. Such association is recommended as a therapeutic measure also.—per *J. Amer. med. Ass.*, i/1939, 2448.

Two cases of anaphylactic shock following administration of a second dose of tetanus toxoid. The incidence of general and local reaction following the subcutaneous inoculation of 61,042 healthy individuals with tetanus toxoid, using two 1 ml. doses at a weekly interval is reviewed. Anaphylactic reaction occurred in 0.003% of cases, less severe constitutional reactions in 0.02%, and local reactions in 1.06%. Though the incidence of general reaction after tetanus toxoid is rare, it is advisable to be prepared to treat it expeditiously with adrenaline hydrochloride when it does occur.—H. E. Whittingham, *Brit. med. J.*, i/1940, 292. A further case described.—H. J. Parish and C. L. Oakley, *ibid.*, 294.

**Tuberculosis.** In spite of the fact that the cause of tuberculosis was proved by Koch in 1882 to be the tubercle bacillus, the value of specific treatment by means of tuberculin is still the subject of dispute. Although some workers consistently maintain that beneficial results may be obtained, in general it may be said that tuberculin is no longer regarded as possessing the high therapeutic value formerly attributed to it.

It is important to remember that tuberculin treatment is only indicated in the early stages of the disease, and that it should never be used in the treatment of exudative tuberculosis with signs of systemic intoxication; the best results have been obtained in extrapulmonary disease, such as glandular or bone and joint tuberculosis.

Owing to the danger of severe reactions following its use, tuberculin must be employed with great caution; indeed, the advocates of tuberculin treatment contend that the poor results often obtained and the relative frequency of severe reactions are due to faulty administration, and that the treatment requires special knowledge and experience.

**Tuberculins.**

There is no consensus of opinion either as regards the proper variety of tuberculin to use or the correct dose to employ. The preparations now described are **Old Tuberculin**, **Albumose-Free Tuberculin** or **T.A.F.**, **Tuberculin T.R.**, **Bacillary Emulsion** or **B.E.**, **Beranek's Tuberculin**, **Raw's Vaccine**, **B.C.G.**, and certain other modifications.

**Tuberculinum Pristinum** (B.P., U.S.P. XI). *Syn.* OLD TUBERCULIN, TUBERCULIN KOCH (P.G. VI).

This is an amber-coloured liquid—a mature glycerin broth culture of the tubercle bacillus concentrated to  $\frac{1}{10}$  its volume, filtered, and diluted to the requisite standard with 50% v/v aqueous glycerin.

*The Therap. Subs. Regns. 1931 and the B.P. specify Old Tuberculin as proper name for this; if with the suffix "T" the tuberculin has been made from a case of human infection, while "P.T." indicates made from bovine infection.*

It has been used (a) as a *diagnostic* both in man and beast (see p. 1085), and (b) for treatment, but is now little used for this purpose. Tubercle vaccine and tuberculin A.F., q.v., replace it.

**Effects of Injection.** The tuberculin seems to act upon the tuberculous lesions, and even partly destroys them—it is not definitely destructive to the tubercle bacilli—or their surroundings, and subsequently there is a risk of further symptoms from blood poisoning dependent on this. The tuberculin may cause a serious fall in blood pressure, leading even to a fatal issue; in other cases there have been congestion and hæmorrhage, or other irritant effects have been produced.

**Contraindications** for the injection are laryngo-tuberculosis, cardiac troubles, diabetes, nephritis and pregnancy. In epilepsy and neurasthenia it should be given with the greatest caution.

The general reaction usually sets in about 8 to 16 hours after the injection—more or less severe attack of shivering, with headache and pains in the limbs.

At the point of injection redness appears after 1 to 2 hours, and gradually an infiltration shows itself, varying in size from that of a farthing to that of half-a-crown, the absorption of which may take several days.

The height of the reaction is indicated by a profuse outbreak of sweating, a lessening of all the other symptoms and a more or less speedy return of the temperature to normal. Generally the entire reaction is over in 24 to 36 hours. There may be slight lassitude, and in the case of phthisis an increased expectoration, disappearing in a few days.

In lupus patients, besides the general reaction, a marked local reaction sets in.

**Unguentum Tuberculin (Old).** Lupus vulgaris has been diagnosed and treated by use of old tuberculin ointment—5% of old tuberculin in a basis of soft paraffin. This is well rubbed in for one to two minutes, and is also



applied by means of a bandage to the affected area—the part being previously cleansed and crusts, if any, removed. On removal of the application, varying degrees of hyperæmia and swelling are seen in the actual lupus tissue, with a moderate amount of hyperæmia with reddish papules extending one or two inches into the surrounding healthy skin (Moro reaction, *q.v.*). After cleaning the surface, similar applications for treatment are made for the next three or four days, till the lesion closely resembles that produced by the application of a salicylic acid plaster. This typical reaction only obtains in the actual disease and does not extend into the surrounding healthy skin. The pain produced may be considerable.

**Tuberculin Ointment (for percutaneous use—Philip).** Tuberculin original (Koch) 10 to 50, eucalyptol 5, Eucerin to 100. Beraneck's tuberculin is also suggested.

Percutaneous exhibition of tuberculin exerts a remarkable influence on the first buddings of tuberculosis in childhood. Continued observations, over long periods, show it is capable of effecting the nearest approach to detubercularisation yet realised. Used as a diagnostic and therapeutic agent, the two-fold aspect must be kept steadily in view. The local stimulation by tuberculin at each tuberculous focus is an important step. When tuberculin is rubbed firmly into the skin of a tuberculous patient it is freely absorbed and exerts a specific curative influence. Generally, a 25% preparation is convenient. In young subjects, or where there is doubt as to the number and extent of foci involved, begin with 10%. The actual amount of tuberculin used in a straightforward case (using, say, 25% dilution), may be approximately 0.1 ml. The ointment containing this quantity is rubbed into the cleansed skin, over an area of 1 or 2 square inches, by means of a small glass rod. Repeat once weekly.—Sir Robert Philip, *Brit. med. J.*, i/1923, 493.

**Tuberculin Liniment.** Tuberculin Old or P.T.O., or equal parts of both, mixed with compound camphor liniment in proportion of 1 to 5 minims to 1 drachm, used for local application, *e.g.*, in abdominal disease or pulmonary tuberculosis. An ointment using anhydrous lanolin employed for lupus or adenitis.

**Tuberculin P.P.D.** The purified protein derivative of old tuberculin. It is issued for use in the form of a dry powder which is dissolved in a special borate buffer solution. It is employed only for diagnostic purposes (in the intradermal reaction or the patch test, *q.v.*). Tuberculin P.P.D. possesses the advantages of constant potency on a weight basis and of greater stability in the dry state.

A comparative study of old tuberculin and the purified protein derivative.—R. M. Seideman, *Amer. J. Hyg.*, 1939, 30, 1.

**Tuberculin Bouillon Filtrate.** *Syn.* TUBERCULIN B.F., T.O.A., TUBERCULIN-ORIGINAL ALT. A germ-free tubercle bacilli bouillon culture, resulting from filtering mature cultures; with or without the suffix T.O.A. or P.T.O., *i.e.*, from human or bovine source.

*Dilutions greater than 1 in 10 do not keep well.*

It has been used in the "dispensary treatment," (p.1082). Asthma and hay fever have been treated with it on empirical lines.

**Vacuum Tuberculin and Vacuum Bovine Tuberculin** are analogous to T.O.A. and P.T.O. concentrated to  $\frac{1}{10}$  volume—for treatment of special cases (not for diagnosis) where a mild effect is desired. *Initial dose.*—0.1 ml. of 1 in 100,000 dilution twice or thrice a week, at most doubling on second occasion. If reaction occurs, 8-day interval after complete abatement of symptoms. Diluent, normal saline with 0.5% of phenol.

**Tuberculin A.F. (ALBUMOSE-FREE) (P.G. VI).**

*Distinguish from diphtheria toxoid-antitoxin floccules, also known as T.A.F.*

*Dose (Initial).*—0.00001 ml. in pyrexial cases; 0.0001 ml.

in *apyrexial* cases. Subsequent doses are determined from a study of the resulting reactions—constitutional, or general and focal. As a rule, reactions should have subsided before more is given.

A light amber-coloured liquid, the product of the tubercle bacillus grown in a special culture medium free from albumoses and peptones, evaporated to  $\frac{1}{10}$  its volume and finally filtered.

This preparation, as already indicated, may replace old tuberculin. It is used as *diagnostic* by conjunctival, intracutaneous and percutaneous application.

*For treatment* it is employed subcutaneously where a fold of skin and underlying tissues can be raised. Reactions obtained are thought to be specific, and anaphylactic symptoms are excluded in consequence of the absence of non-specific proteins.

**Tubercle Vaccine.** This is the proper name under the *Therap. Subs. Regns.* 1931 for preparations made from the bacillary substance by growing the organism on artificial media. They are suspensions of the killed organisms or products derived from them, and are often referred to as "New Tuberculin."

**Vaccinum Tuberculinum (B.P.C.).** *Syn.* TUBERCLE BACILLARY EMULSION, B.E.

The original "new tuberculin" of Koch. Human type, bovine type, or the two mixed, are available.

*Dose.*—0.00001 to 0.00002 ml. as a rule to begin with. The dose is increased carefully at a rate which causes little or no rise in temperature ( $1^{\circ}\text{F.}$ ), and with intervals of about 1 week. With the small initial dose stated it is very exceptional for any reaction to appear. Should a rise occur, the dose should not be exceeded until the temperature has reached its previous level.

As proof of the immunising properties of his T.R. and other preparations, Koch demonstrated the production of specific immunising bodies, which he called *agglutinins*. The difference between B.E. and T.R. is that B.E. contains the *entire body substance of tubercle bacilli*, whilst with T.R. the *soluble constituents* of the bacillus are first rejected. The soluble endotoxins are thought to play an important part in the production of agglutinins and are contained in B.E.

*B.E. is, therefore, a suspension of entire pulverised tubercle bacilli in a mixture of equal parts of glycerin and water. 1 ml. contains 5 mg. of thoroughly dried tubercle bacilli.*

The bacilli, grown on a solid medium, are pulverised by prolonged grinding in a ball mill. Before grinding they may be either alive or killed by heat. The powdered product is emulsified in normal saline and diluted so that 1 ml. contains 5 mg. of powdered bacilli. A 1% dilution of the original is sometimes called "Dilution No. 1," a 0.1% is No. 2 and so on.

*Bold dosage* was advocated by the German school. Starting with the same initial dose (0.00001 to 0.00002 ml.), at 1 or 2 days' interval, the dose was rapidly increased from twice to 5 times the dose at each injection, until definite reaction appeared

with a rise of  $2\frac{1}{4}^{\circ}$  to  $5^{\circ}\text{F.}$  in temperature. As soon as such violent reaction developed, much longer pauses, 6 to 8 days, were made. The injections were increased to 4 ml. undiluted B.E. Koch regarded the immunisation as complete only when the patient could tolerate this without reaction. The larger doses of 2 to 4 ml. were only injected at intervals of 2 to 4 weeks.

In exceptional cases (*English dosage*) the initial dose may be as minute as  $\frac{1}{1000000}$  mg. bacillary substance with gradual rise—the limit being  $\frac{1}{100}$  mg. of bacillary substance ( $= 0.0004$  ml.). *Average doses* are respectively  $\frac{1}{100000}$  mg. ( $= 0.00001$  ml.),  $\frac{1}{10000}$  mg. and  $\frac{1}{1000}$  mg. diluted in 1 ml.

### **Tuberculin T.R. Human, Bovine and Mixed Types.**

*Dose.*—Initial (subcutaneous), 0.00001 to 0.0001 ml. according as the case is pyrexial or not, rising gradually to 0.2 or even 1 ml. Dilutions are made in 1 ml., using 20% glycerin as diluent.

*N.B.*—*Doses should be stated in decimals and by no other method.*

Although a stereotyped increase of dose is not advised, the following scheme will be useful as a guide (reading downwards in each column):—

0.00001 ml.	0.0001 ml.	0.001 ml.	0.01 ml.
0.00002 "	0.0002 "	0.002 "	0.02 "
0.00003 "	0.0003 "	0.003 "	0.03 "
0.00004 "	0.0004 "	0.004 "	0.04 "
0.00005 "	0.0005 "	0.005 "	0.05 "
0.00006 "	0.0006 "	0.006 "	0.06 "
0.00008 "	0.0008 "	0.008 "	0.08 "
			0.1 "
			0.2 "

*As a rule weekly injections are given.*

Several commercial preparations made on the lines of Koch's directions for T.R. are available.

**T.R. of Koch** contained 2 mg. of solid substance, *not* 10 mg. as originally stated. It may be recalled therefore that:—

0.00001 ( $\frac{1}{1000000}$ ) ml. of T.R. = 0.00002 ( $\frac{1}{50000}$ ) mg. (or 0.00000002 g.) of solid substance.

*Bold dosage.*—The large doses advised by Koch, starting from 0.0002 ml. and repeated every second day with moderate increase of dose so that a rise of temperature greater than  $0.9^{\circ}\text{F.}$  was avoided, are not now generally administered.

The *English School* start with smaller initial dose (as already outlined) and do not look for any marked rises in temperature.

**Tuberculosis Immunising Vaccine (Nathan Raw).** *Syn.* TUBERCLE VACCINE "R." Raw states that virulent tubercle bacilli—after years of subculturing—can be attenuated. In his opinion this remedy should be of greatest value, not only in curing the disease, but also in its prevention, by protecting the human body against attack. Cattle can be rendered immune to virulent bovine bacilli by previous inoculation with virulent human bacilli. There is a marked antagonism in the human body between human and bovine infections. These two organisms cannot flourish in the body at the same time.

Extended clinical investigation at Liverpool showed that the human body is attacked by two quite distinct forms of tubercle—the one conveyed by direct

infection and attacking chiefly the lungs (so-called consumption); the other, the surgical form, conveyed by milk from tuberculous cows and developed in the first few years of life. A vaccine made from bovine cultures should be used in the treatment of human infections and *vice versa*.

**Raw's Vaccine** is a bacillary emulsion of the bacilli containing all the products of the bacillus. It is non-toxic and avirulent, and produces no reactions even in large dose.

*Dose*.—0.001, 0.002, 0.003, 0.004, 0.005 and 0.006 mg. for immunising susceptible children at weekly intervals, repeated in three months.

For treatment of the active disease, commence with 0.001 and increase to a maximum of 0.025 mg. Twelve injections should be given at intervals of seven days. Vaccine should be freshly made.

### General References to Use of Tuberculin in Treatment.

If tuberculin were entirely useless it would have been discarded long ago, and would not be the subject of serious discussion 42 years after its introduction. It has definite therapeutic uses—considerable in localised and surgical manifestations; strictly limited in pulmonary forms.—R. A. Young, *Brit. med. J.*, ii/1932, 1091.

Contraindicated in active, spreading, caseous disease, or with continuous remittent or intermittent fever.—R. A. Young, Sect. of Tuberculosis, B.M.A. Cent. Meeting, 1932, *Brit. med. J.*, ii/1932, 316.

Of 267 tuberculosis specialists replying to a questionnaire only 5 used tuberculin as the main form of treatment. The majority counselled against its use in all but quiescent or slightly active cases, and 63 reported harmful results.—L. Hektoen and E. E. Irons, *J. Amer. med. Ass.*, i/1929, 869.

**TUBERCULOUS ASTHMA** can be ameliorated or cured by the following technique. Commence with 0.1 ml. of tuberculin liniment (*see p. 1079*) and double weekly till 1 ml. is given. A tuberculin rash often appears in due course at the site of application, usually accompanied by amelioration of the asthma. If not, proceed to injections, commencing with T.A.F. 0.0001 ml. and increasing weekly. If reaction or an attack of asthma ensues, return to the liniment.—F. E. Gunter, *Brit. med. J.*, i/1929, 575.

**TUBERCULIN DISPENSARY TREATMENT.** Only early or suspected cases are suitable for this form of—Dispensary—treatment. The treatment should be refused to all presenting evidence of mixed infection.

None but experts should give tuberculin for diagnosis or treatment, and not even the best qualified medical practitioner should use it in treatment without at least three months' training at a tuberculin dispensary. The scientific method has not had a fair trial in any country, because it is highly technical, difficult to learn, to teach, and to practise, and its evaluation demands exacting conditions; leading men had rejected Koch's work and teaching because they have never seriously investigated it under these conditions. Wrong doses have been given in the wrong way at the wrong time, and in the wrong cases. Experiences at the tuberculin dispensary in London showed that in all patients in Stages I and II, where tubercle bacilli were found in the phlegm, 68% were alive at the end of 8 to 10 years, and 70% able to follow their ordinary occupations; the L.C.C. results in similar cases, under sanatorium treatment, were 28% alive at the end of four years. The advocacy of tuberculin, both as a diagnostic and curative agent, rests on facts that cannot be impeached.—W. Camac Wilkinson, *Brit. med. J.*, ii/1928, 444.

From a study of his papers his usual treatment is first a course of P.T.O., then P.T. (may be repeated courses), then Tuberculin Old—or more recently Tuberculin A.F.

**B.D.H. Tubercle Endotoxoid** (*British Drug Houses, London*). A preparation of the tubercle bacillus from which the toxicity has been eliminated. For use in the treatment of all forms of tuberculous infection. *Dose*.—0.05 ml. subcutaneously, increasing to 1.5 ml. The following system of dosage is advised: first week, two doses of 0.05 ml.; second week, two of 0.1 ml.; then increase by 0.1 ml. weekly until two doses of 0.5 ml. weekly are given.

In the majority of cases, either no reactions or only very mild ones follow administration, and a definite therapeutic action, which is antitoxic, progressive and durable, takes place. There are no contraindications.

It may also be employed to produce active immunity in hospital attendants and other contacts.

**"B.C.G." (Bacille Calmette-Guérin)**, a strain of tubercle bacillus grown on glycerinated ox bile, first described by Calmette in 1909, was subcultured 230 times up to January, 1921, when vaccination experiments were started, and was then incapable of producing tubercles. Caused a general disease in calves resembling typhoid fever, clearing spontaneously after 15 to 20 days without producing slightest tubercle formation. "B.C.G." now cultivated on potato and glycerinated veal broth or Sauton's Asparagin medium; cultures must not be more than 10 days old. It is employed for the prophylactic vaccination of the newly-born against tuberculosis, and is administered in milk at body temperature in three doses. It is harmless even in new-born infants.

The method has been widely employed on the Continent, and especially in France, but has so far not met with any favour in this country.

Destructive criticism of B.C.G. Figures unsatisfactory. Calmette's claims "optimistic."—*Brit. med. J.*, i/1928, 364.

Prophylactic inoculation of adults with B.C.G.—*Lancet*, ii/1928, 931.

Prof. Calmette's statements on B.C.G. to Roy. Soc. Med. The untreated child is auto-vaccinated by milk, food, dust, etc. In Calmette's method an attenuated strain (230 passages) of living organisms is employed. Mention of first child treated (born of tuberculous mother and grandmother): 10 years after the child is healthy and well.—*Brit. med. J.*, i/1931, 1070, 1080.

Reasons for absence of official support for B.C.G. vaccination in Great Britain, as submitted to the Office International d'Hygiène Publique (Paris) by Sir George Buchanan, and Professor Calmette's reply.—*Lancet*, i/1933, 653.

**B.C.G. in America.** After eight years' experience of B.C.G. vaccinations in America, C. Kereszturi and W. H. Park state that they are able to substantiate Calmette's claim that B.C.G. vaccine is harmless in humans, provided they are free from tuberculous infection, and that it is effective in the prevention of tuberculosis in children. Intracutaneous or subcutaneous injection is superior to oral administration. They urge that B.C.G. vaccine should be used as a public health measure in the prevention of tuberculosis in children of tuberculous families, and that it should be given as early as possible. Oral vaccination may begin within 10 days of birth, three 10 mg. doses being administered at two-day intervals. The parenteral method may be used on patients of any age with a negative tuberculin test.—*Amer. Rev. Tuberc.*, Oct. 1936, 437.

After sufficient trial the veterinarians of America have not adopted B.C.G. as a satisfactory method of prevention. They have had a better opportunity to observe the effects of B.C.G. on cattle than we could ever hope to have on human beings. The veterinarian's experience and his record of success in controlling tuberculosis should discourage every physician from administering B.C.G. to children. Certainly a preparation that the veterinarian considers unsafe and ineffective for cattle should not be used in an experimental way on the children of the United States. To prove the efficaciousness of an immunising agent for tuberculosis in the human body would require decades.—F. E. Harrington, J. A. Myers and N. M. Levine, *J. Amer. med. Ass.*, i/1937, 1315.

**B.C.G. in France.** Statistics show a striking difference in the tuberculosis mortality in France existing between infants who have been vaccinated by the method of Prof. Calmette and those not so vaccinated. The procedure is to give 3 doses, each of 10 mg. of a non-virulent strain of tubercle bacilli during the first 10 days of life, and the figures represent the mortality calculated on each of the first two years of life.—Editorial, *Brit. med. J.*, i/1927, 845. See also *ibid.*, 897, 1082, in which limitations in the value of the statistics are suggested by M. Greenwood.

In France one child out of every five is inoculated within the first week of life with B.C.G. vaccine, the average number of vaccinations each month being 10,700. Outside France more than half a million children have been vaccinated. The general mortality, including all traumatisms as well as diseases, is 4.6% in the vaccinated against 25% in the non-vaccinated during the first year. It

is perfectly safe to revaccinate at 1, 3, 5 and 7, such children as are specially menaced.—*per J. Amer. med. Ass.*, i/1933, 130.

**B.C.G. in Rumania.** During the past 12 years there have been some half million vaccinations in Rumania. The main conclusions reached are that it appreciably reduces the tuberculosis mortality among children and that the tuberculosis morbidity is also reduced. At present about 70% of the babies in Bucharest are given B.C.G. at birth. The tuberculosis mortality during the first year of life is said to be 1.3 per 1000 among the B.C.G. babies, compared with about 4 per 1000 among the others.—*Lancet*, i/1939, 524.

**B.C.G. in Sweden.** From 1927 to 1937, 13,103 babies were given B.C.G. at birth, the vaccine being given by the mouth in three successive doses as a voluntary measure. The conclusion reached is that B.C.G. vaccination has seemed to affect a remarkable diminution in the tuberculosis deaths, and there has also been an obvious fall in general mortality among the vaccinated.—*Lancet*, i/1939, 39.

**B.C.G. Vaccine (Pasteur Institute, Paris).** B.C.G.: for oral administration soon after birth, 1 cg. bacilli in 2 ml. B.C.G.-NR: for oral use in children over 2 years and in adults, 5 cg. bacilli in 10 ml. B.C.G.-SC: for subcutaneous injection,  $\frac{1}{10}$  cg. in 2 ml.

*The following additional (unclassified) preparations are also used:—*

**Beraneck's Tuberculin** consists of a mixture of tubercle-broth filtered free from bacilli and concentrated *in vacuo*, with an extract of the bacilli made with phosphoric acid. It is stated to contain exotoxins and endotoxins and acts like a vaccine, strengthening the bacteriolytic power of the protective cells; it also exercises a bactericidal or attenuating effect on the tubercle bacillus.

It is supplied in 6 dilutions, T.Bk, to T.Bk<sub>6</sub>, viz. 1:10 to 1:1,000,000 for use.

**Spahlinger's Tuberculosis Vaccine.** A bovine vaccine for cattle immunisation and a harmless vaccine for human prophylaxis. Tubercle bacilli for making the vaccine are grown under environments of food, heat, etc., natural to the disease. They are emulsified with normal saline in the absence of oxygen, then placed in ampoules and kept in the cold and dark for a year or longer and allowed to die a natural death. They thus retain unimpaired the chemical and physical structure by reason of which they are effective vaccinating agents. This replaces customary animal passage from human beings and subsequent culture on artificial media, different from the original environment which, it is claimed, alters the character of the organism. It is held that a vaccine made on the latter lines cannot deal with the disease in an animal of the group from which it was originally taken.—*Brit. med. J.*, i/1932, 252.

Tests carried out under the supervision of the Government in Northern Ireland. A new simplified vaccine conferred a high degree of resistance against massive intravenous injection of tubercle bacilli.—Abstract from the report, *Vet. J.*, 1935, 423.

**Vole Bacillus Vaccine.** An investigation into the cause of the periodical waves of high death-rates of voles showed it to be due to a disease resembling partly tuberculosis and partly rat leprosy. The disease was found to be due to tubercle bacilli closely related to the human and bovine types, but distinct from them, highly virulent for voles, but relatively avirulent for guinea-pigs and rabbits. Experiments on guinea-pigs showed the protective power of a vaccine prepared from this organism to be much greater than that afforded by B.C.G. Further work is proceeding on monkeys and cattle.—*Brit. med. J.*, ii/1940, 261.

### Tuberculin Reactions for Diagnosis.

Of the various tuberculin reactions employed for the diagnosis of tuberculosis, the best known are the subcutaneous test (Koch), the cutaneous test (von Pirquet), the intradermal test (Mantoux), and the percutaneous test (Moro). Of these, the one now most widely employed is the intradermal test, though the Vollmer patch test recently introduced is rapidly finding favour. The subcutaneous test is now seldom used in human beings owing to the dangerous reactions to which it may give rise.

**Subcutaneous Test.** *The test in the human being.* An initial dose of 0.2 ml. of a 1 in 1000 dilution of old tuberculin is injected subcutaneously. If no rise of temperature follows, give 1 ml. of a 1 in 1000 dilution at least 48 hours later. If again no rise of temperature occurs give 0.5 ml. of a 1 in 100 dilution. Finally, if necessary, 1 ml. of a 1 in 100 dilution. A rise of 2.3°F. or more occurs in tuberculous subjects some 6 or more hours after the injection of tuberculin.

While Koch's subcutaneous test is definitely inapplicable to persons with pyrexia, and is unsafe in those with lesions of the easily-activated type, the chronic, productive, inert, sputum-negative cases stand the test well, the risk is not serious. Koch's test remains the most valuable in diagnosis; the only thing against it is its risk.—S. L. Cummins, *Brit. med. J.*, ii/1932, 1090.

*The test for veterinary use.* The animal is confined to its stall for 24 hours before the injection is made, and its temperature observed. 3 to 4 ml. of a 1 in 10 dilution is injected subcutaneously in the neck. The temperature is taken 6, 9, 12, 15, 18, 24 and 36 hours after inoculation. If there is a rise of temperature of 1.4°C. or more the animal should be regarded as tuberculous. With a rise of temperature from 0.8° to 1.4°C. the diagnosis is doubtful, and the test should be repeated after 1 month. This test has been proved to be of the utmost value for the diagnosis of tubercular infection in cattle. Occasionally in animals with advanced infection the test is negative. In these cases, however, the diagnosis can usually be arrived at by other means. In a few cases, in animals suffering from echinococcus infection, a slight positive reaction has been obtained. After a dose of tuberculin in cattle, a further dose during 6 months may fail to produce a rise in temperature again.

**Tuberculin Committee's Report.** Tuberculin tests in cattle. Subcutaneous test unsatisfactory under farm conditions, and ophthalmic test only regarded as subsidiary. Complete confidence in intradermal test.—*Brit. med. J.*, i/1925, 797.

**Cutaneous Test (von Pirquet).** Cleanse the inner side of the forearm with ether and alcohol. Make two similar scratches with a sterile needle 3 inches apart (avoid drawing blood). On one scratch place a drop of 1 in 4 old tuberculin in sterile water (pure old tuberculin is sometimes used); keep the other scratch as a control. Examine at 12, 24 and 36 hours. A positive reaction occurs in from 3 to 24 hours, and is usually at its height at 36 to 48 hours. The skin becomes red and slightly raised on each side of the scratch over an area 10 mm. broad; reactions under 5 mm. should be regarded as doubtful.

**Intradermal Test (Mantoux).** For this test 0.1 ml. of diluted old tuberculin is injected intradermally, employing a fine needle. For the initial dose a 1 in 10,000 dilution in 0.5% phenol-saline is used. If this fails to cause a positive reaction, consisting of an area of erythema not less than 5 mm. in its greatest diameter in 48 to 96 hours, the test is repeated with a 1 in 1000 dilution, and if again negative with a 1 in 100 dilution, and finally with a 1 in 10 dilution. In practice, the initial dose of 1 in 10,000 is often omitted.

Alternatively, Tuberculin P.P.D. in the same doses and dilutions may be substituted for old tuberculin with equally good results.

The usual technique is to inject 0.1 ml. of 1 in 1000 old tuberculin intradermally. Extremely valuable in children. Negative result excludes tuberculosis, strongly positive suggests active tuberculous disease with bad prognosis, and mildly positive suggests tuberculous infection amenable to open-air treatment.—W. F. Gaisford, *Lancet*, i/1931, 521.

The von Pirquet test is the simplest and easiest for infants and young children: if negative, an intradermal test with 1 in 100 dilution should be carried out; in older children repeat the test, if still negative, with 1 in 10. The Mantoux Test (1 to 10 dilution) should always be carried out with a control injection of the broth used for the preparation of tuberculin. Pirquet test only positive when there is at least 1 mm. of erythema each side of scarified area, and the minimum for a positive Mantoux is an area of erythema 10 mm. in diameter, with swelling to the touch or a well-defined erythema greater in area than this. An erythema of 5 mm. or more should be regarded as doubtful, reinspected on the fourth day and, if still doubtful, the test repeated with a stronger dilution. Instead of maintaining the controversy as to the relative values of the Pirquet and Mantoux tests they should be combined as a routine (first Pirquet, followed by Mantoux 1 in 100).—G. G. Kayne and B. Weill-Hallé, *Brit. med. J.*, ii/1934, 468.

As a test for "active clinical tuberculous disease" the cutaneous and intradermal tests are too delicate. "Positive" reactions in adults cannot be interpreted to mean "active" tuberculous disease. A markedly positive reaction has, however, *serious significance during the first year of life*: the value of a "negative" may be very great, especially in childhood, but it is insufficient to stop short at a von Pirquet test, even with full strength tuberculin, or at a Mantoux with 1 in 1000 tuberculin, as many persons negative to these concentrations are found positive with 1 in 100 or 1 in 10.—S. L. Cummins, *Brit. med. J.*, ii/1932, 1089.

The purified protein derivative of tuberculin is recommended for diagnosis by the intradermal test in place of old tuberculin. It is recommended that the initial dose should be 0.00002 mg. of the P.P.D., and that 0.005 mg. be given as a second dose to those who fail to react to the first dose.—*Amer. Rev. Tuberc. Suppl.*, ii/1934, 708.

A report on 3010 tests (using 0.1 ml. of 1 in 1000 old tuberculin). An analysis of the tests suggests that the diagnostic value of the Mantoux test is under-rated, especially in older children. The test enables a diagnosis of tuberculosis to be excluded in three "suspect" cases out of four up to 8 years of age, and in one half of those aged from 10 to 12.—D. B. Bradshaw, *Brit. med. J.*, i/1939, 825.

Clinical trials were instituted in order to compare the diagnostic value of O.T. and P.P.D., 119 persons being tested at comparable sites on each forearm. An appreciably greater percentage of positive reactions was obtained with P.P.D., indicating slightly greater potency in this product as well as greater stability. The reactions obtained from P.P.D. are similar in character to the response to O.T., and they are clear-cut and easy to interpret. P.P.D. is the most suitable reagent for use in the application of the Mantoux test.—A. T. Doig *et al.*, *Brit. med. J.*, i/1938, 992.

**Percutaneous Test (Moro).** An ointment made of lanolin and old tuberculin in equal parts is rubbed on to the skin of the chest. A positive reaction is shown by the development of reddening and papules. The test has the disadvantage that one cannot ensure that the same amount of tuberculin is absorbed in successive tests.

**The Vollmer Patch Test.** The patch consists essentially of a small strip of adhesive plaster, 4 inches by 1 inch, on which are set three squares of filter paper. The two outer squares have been saturated with undiluted old tuberculin, the centre with glycerin broth to act as a control. An area of skin over the sternum, or in the intercapsular region, is cleansed with ether or acetone, allowed to dry and the patch applied and left in place for 48 hours, washing of adjacent parts during this period being avoided. The strip is then removed and the result read after a further 24 hours. A positive reaction may appear as a sharply circumscribed, indurated and reddened square set with small vesicles, the central square remaining unchanged. The reaction, however slight within the limits of the test squares, is significant.



The test approaches in reliability the intracutaneous method of Mantoux. It is simple and causes no local or general reaction.—D. Court, *Brit. med. J.*, i/1939, 824.

In a series of 744 cases in which the Vollmer patch test was compared with the Mantoux test, using 0.1 mg. O.T., the results indicate that the simpler Vollmer test is equally as effective as the Mantoux test, and possesses many advantages for the physician as well as for the patient.—G. Taylor, *Amer. Rev. Tuberc.*, 1939, 40, 236.

In the tuberculin patch test old tuberculin is decidedly superior to purified protein derivative.—H. Vollmer and E. W. Goldberger, *Amer. J. Dis. Child.*, 1939, 58, 527.

From observations on 712 school children it was concluded that the tuberculin patch test has a high degree of correlation with the Mantoux test and appears to give 7% more positives than the Mantoux. It is the method of choice in large-scale tuberculin testing, especially for children.—A. J. Pearse, *J. Amer. med. Ass.*, i/1940, 227.

**The Copenhagen Patch Test.** The Tuberkulin-salve of the Danish State Serum Institute is a mixture of old tuberculin and purified tuberculin, standardised at three times the international standard, and put up in tubes containing 4 ml. An amount sufficient to cover a threepenny piece is squeezed on to a piece of adhesive tape 1 inch square, and applied to the skin below the right clavicle, after cleansing with acetone. The plaster is removed in 24 hours and read in a further 24 to 48 hours. As a control a simple piece of plaster is applied below the left clavicle. There is little to choose between this and the Vollmer patch test, and a combination of patch test and Mantoux is suggested as best calculated to spare the child and the physician, and to give as few false reactions as possible.—F. D. Hart, *Lancet*, ii/1938, 609.

## Typhoid.

**Vaccinum Typho-Paratyphosum** (B.P., U.S.P. XI). *Syn.* ANTI-TYPHOID-PARATYPHOID VACCINE, T.A.B. VACCINE.

Is made from cultures of typhoid and paratyphoid A and B organisms, containing 1000 million of *B. typhosus* and 500 million each of *B. paratyphosus A* (U.S.P. XI—*Salmonella paratyphi*) and *B. paratyphosus B* (U.S.P. XI—*Salmonella schottmülleri*) in each ml. F.E. VIII specifies 1000 million *B. typhosus* with 750 million of each paratyphoid organism.

**Dose.**—For immunising, two doses are given, 0.5 and 1 ml., at intervals of not less than 7 days; an interval of 10 days is to be preferred. (Some give three doses, 0.25, 0.5 and 1 ml., and the interval between doses may be extended to 14 days.) The dose is given *subcutaneously* into the tissues of the upper arm just below the insertion of the deltoid. The patient should take no alcohol whatever during the 24 hours preceding and after the injection.

For children the dose should be proportional to age. Thus a child of 7 would receive one-third of the average dose.

There is no sound reason why prophylactic antityphoid inoculation should not be given to children aged 2 years and upwards, a diluted vaccine being used.—Col. H. M. Perry and co-workers, per *Lancet*, i/1934, 584.

**Contraindications.** Alcoholics react more strongly than others. Kidney disease requires caution, and there is possibly slight risk in the case of old-standing tuberculosis.

**Effects.** Tenderness at the site of inoculation is at its worst in about 18 hours. Redness may be caused. Give free use to the arm the day after injection. Malaise begins in about 6 hours. Occasionally a rigor. There is usually headache and a slight

degree of pyrexia. Occasionally temperature up to 101°F., rarely 103°F.

The immunity created by prophylactic inoculation with T.A.B. vaccine remains at a high level for at least 6 months—probably for 12 or 18 months, and should an inoculated person contract the disease its severity is diminished and the percentage mortality lowered.

T.A.B. inoculation leads to the production of a considerable amount of O antibody. In the case of *B. paratyphosus A* this response is not evident to the same extent as that for the other two organisms. A fundamental difference exists between primary and secondary response to T.A.B. inoculation in human beings. With a primary stimulus the maximum rise of O antibody titre falls significantly short of that obtained with secondary and subsequent stimuli. It is therefore suggested that the second T.A.B. inoculation should be practised at the end of six months. In those individuals who have had multiple inoculations, the O agglutinin titre remains fairly high for 12 months only. The desirability of repeating T.A.B. inoculation every year is therefore stressed.—S. S. Bhatnagar, J. F. Freeman and J. C. S. Dhillon, *Indian J. med. Res.*, 1937, 24, 597.

**Anti-Typhoid Vaccine (plain)** is also made.

*Dose.*—1000 million and 10 days later 2000 million.

**Vaccinum Typhosum (U.S.P. XI)** contains not less than 1000 million bacilli per ml.

**Anti-Typhoid-Paratyphoid A and B and Cholera Vaccine.** (*This name should not be abbreviated to T.A.B.C. Vaccine.*)

*1st dose.*—500 million *B. typhosus*, 250 million each of *B. paratyphosus A* and *B* and 1000 million *Vibrio cholerae*; *2nd dose*—10 days later, twice these quantities.

**Castellani's Tetra-Vaccine** contains:—(No. 1) 1 ml. contains 500 million *B. typhosus*, 375 million each *B. paratyphosus A* and *B*, also 5000 million *Vibrio cholerae*; (No. 2) contains double quantities of No. 1 per ml.

*Dose.*—1 ml. of No. 1, followed by 1 ml. of No. 2, after customary interval.

**Typhoid Endotoxoid Vaccine.** This vaccine consists of *B. typhosus* endotoxin extracted from concentrated heated bacterial emulsions by means of an alternate freezing and thawing process. The toxic soluble antigen, separated by centrifuging, is subsequently transformed into an atoxic product which still retains its original immunising properties. Finally, it is diluted for use to an antigenic concentration corresponding to that extracted from 5,000,000,000 to 6,000,000,000 organisms of the original emulsion, i.e., to 1.5 to 1.8 mg. of the dry bacilli, as the standard concentration, and up to 8,000,000,000, i.e., 2.4 to 2.5 mg. when the single inoculation method is contemplated. A single injection is sufficient to produce in man an agglutinin titre as high as 1/10,000 H and 1/5000 O without undue reaction.

5445 workers out of a total of 6652 (in S. Africa) were submitted to this single inoculation during the period September 1936 to July 1937. Only one non-fatal case of typhoid has been noted among these inoculated subjects during the year following the immunisation, while 8 cases with 2 deaths were recorded among the small proportion of non-inoculated workers.—E. Grasset, *Brit. med. J.*, ii/1939, 58.

**Anti-typhoid Vaccine for Treatment.** *Dose.*—50, 100, 250, 500, 1000 and 2000 millions. An initial dose of not less than 250 millions can be safely used—these to be repeated or increased under guidance of the clinical signs and symptoms. It might be of value to give a vaccine of *B. coli* and *Streptococci* to raise the immunity against these organisms before they can take an active part in the process of destruction of the tissues (as in the later stages of typhoid).

**Oral Typhoid Vaccine.** The oral administration of typhoid vaccine, in accordance with Besredka's theory of local immunity,

has been widely employed on the Continent and in S. Africa and the Far East. The usual course consists of three successive daily doses each of 50,000 million *B. typhosus*, and 25,000 million each of *B. paratyphosus A* and *B. paratyphosus B*, taken simultaneously with a 3-grain keratin-coated ox-bile tablet. The special claims made for it by its advocates are its ease of administration, the absence of a negative phase, and the fact that it does not give rise to unpleasant sequelæ. In spite of its extensive employment in various parts of the world, it has not found any great measure of favour with British workers who, in general, consider that, if employed at all, it should be reserved for special circumstances.

A variation of Besredka's typhoid immunisation by oral administration of a vaccine is used by the S. African Institute for Medical Research, and thousands of natives have been vaccinated by this method, which consists in giving *per os* a liquid suspension of killed *B. typhosus* and *B. paratyphosus A* and *B*, and simultaneously a pill of ox bile. No unpleasant reaction or malaise is stated to follow, and immunisation is supposed to be as efficacious as by the hypodermic method.—*Brit. med. J.*, ii/1927, 1050.

Vaccine therapy *per os* effective for typhoid. Of 4410 men treated with oral antiviral, preceded by bile, not one developed typhoid in the Rhine Army, while of 549 treated without bile 0.07% were affected. The method prevents the gradual encroachment of *B. typhosus* on cells still healthy and cuts short the period of illness.—Prof. Besredka, *Lancet*, i/1929, 1092.

Oral immunisation against typhoid in S. Africa at least equal to subcutaneous injection—quicker effect.—E. Chiver, *Lancet*, i/1929, 1302.

Typhoid vaccine administered orally produces as great or greater concentrations of agglutinin bodies in the blood serum of human beings as typhoid vaccine administered subcutaneously, and the concentration is brought about in a shorter time and without any reaction. Economically and practically, the oral vaccine is more desirable than the subcutaneous.—H. D. Moor and I. L. Brown, *J. Lab. clin. Med.*, 1937, 1223.

From a review of the work done on oral vaccination against the enteric fevers, the following conclusions emerge: (1) on the evidence at present available it is very difficult to maintain that oral vaccination can be seriously considered as an alternative to vaccination by the subcutaneous route; (2) oral vaccination may, however, be regarded as worth trying when the choice is between that and nothing.—A. Fleming, *Brit. med. J.*, ii/1939, 100.

**Anti-typhoid Serum (Felix).** The factor present in virulent strains of *B. typhosus*, and responsible for their virulence and inagglutinability, is an antigen. This antigen is distinct from the O and H antigens of *B. typhosus*, and renders the O antigen resistant to the action of the O antibody. The symbol Vi (referring to virulence) has been suggested for this antigen and the corresponding antibody. Active and passive immunisation disclose the powerful protective action of the Vi antibody. The O antibody, which is known to exert bactericidal and opsonising effects, also neutralises the endotoxin of *B. typhosus*, whereas the Vi and H antibodies are incapable of this action.

Anti-typhoid sera containing O and Vi antibodies exert two separate and distinct effects: (a) the Vi antibody confers protection against infection with highly virulent strains of *B. typhosus* by suppressing the multiplication of the organisms; (b) the O antibody appears to be chiefly responsible for effecting the neutralisation of the endotoxin of *B. typhosus*.

The therapeutic dose for adults is 25 ml. intramuscularly as soon as possible after diagnosis has been confirmed; in severe cases this dose should be repeated twice at intervals of 24 hours; and in cases of extreme severity three injections of 25 ml. each may be given on three consecutive days, intravenously or intramuscularly. For children under 5 the dose is 5 ml., from 6 to 9 years 10 ml., and from 10 to 14 years 15 ml.

As a prophylactic for the conferring of immediate protection, one intramuscular injection of 25 ml. is given (children *pro rata*).

Of 8 cases treated with this new serum, 7 ceased to cause anxiety within a few days of receiving the last dose, the only failure was the case receiving a very inadequate dose, who died from a local complication.—C. J. McSweeney, *Lancet*, i/1935, 1095.

During the Bournemouth outbreak of 1936, Felix anti-typhoid serum was given to 73 patients, of whom 55 were classified as severe or very severe cases. In 73% of cases there was improvement within 48 hours of the injection, and in a further 10% some benefit was noted after a few days. 7 of the patients died, and 6 of these deaths were in patients treated later than the third week of the disease; only one patient died among 33 treated during the first three weeks, and in this case the dose of serum (13 ml.) was inadequate. For sporadic cases or small outbreaks, where the numbers do not admit of proper controls, the evidence so far available warrants the administration of serum at the earliest possible moment and in full doses, irrespective of the severity of the disease.—H. Cookson and R. V. Facey, *Brit. med. J.*, i/1937, 1009.

In the majority of cases so far treated (61), the Felix serum has been found beneficial, sometimes dramatically so. In not less than one-third of the serious cases the results were excellent, in another third they were definitely good, and in the remaining third they were doubtful or negative. Complications were exceedingly rare in serum-treated cases.—C. J. McSweeney, *Brit. med. J.*, ii/1937, 1118.

The titre of the Vi antibody in the concentrated anti-typhoid serum as issued at the present time is 1 in 3000. Until serum with a considerably higher content of this antibody can be prepared, it is recommended that for prophylactic use one intramuscular dose should be given, lying between the limits of one-third and one-sixth of the full curative dose, which is 99 ml. for an adult and proportionately less for a child. When deciding on the dose the degree of risk and length of exposure to the infection should also be taken into account.—A. Felix, *Brit. med. J.*, i/1938, 1091.

At the present time the value of anti-typhoid sera prepared from the horse is still *sub judice*, and there is no evidence that the mortality is reduced by their use. The danger of a prejudicial disturbance of the delicate mechanism of immunity in the human subject appears to outweigh the possibility of benefit.—Sir W. Willcox, *Brit. med. J.*, i/1938, 1085.

The prophylactic use of anti-typhoid serum prepared by Felix's method in a localised outbreak. The serum was given to 31 contacts, 10 ml. for an adult and 5 ml. for a child, intramuscularly. No case of typhoid occurred among these contacts, though this is not considered a proof that the serum did actually prevent the onset of typhoid in any of these people.—J. Fenton and C. P. Hay, *Brit. med. J.*, i/1938, 1090.

**Variola.** Smallpox is a virus disease for which there is no specific treatment, but vaccination with calf lymph diminishes the liability to attack, and when the latter does occur the disease is milder and less fatal. Protection against attack is greatest during 9 or 10 years after vaccination, though it is still efficacious for a further period of five years. Smallpox is now a very rare disease in this country—there were only 18 cases notified in 1938.

**Vaccinum Vaccinæ (B.P.).** *Syn.* VACCINUM ANTIVARIOLUM, VACCINE LYMPH, VACCINUM VARIOLÆ (U.S.P. XI), VACCINO

ANTIVAIOLOSO, VACCINO JENNERIANO (*P. Ital. V*), VACCINUM ANTIVARIOLICUM (*P. Belg. IV*).

The substance obtained from the vesicles produced by inoculation of vaccinia virus on the skin of healthy animals.

To meet the requirements of the Therap. Subs. Act, 1925, the animals used must be healthy, the animal after lymph collection must be examined *p.m.*, the lymph must be treated with glycerin or other partial disinfectant (*v. postea*), it must be continuously in cold storage at below 0°; each tube must contain enough for one human subject. A label on the box or carton must show the proper name, name and address of maker, number of licence, a distinctive batch number, the date of completion of manufacture after testing for organisms, and a statement that the potency cannot be relied on for more than 7 days unless it is kept at below 10°.

In emergency a larger amount may be issued in sterile containers of larger dimensions.

The seed lymph used in this country is derived from calf lymph received from Cologne in 1907, its quality being maintained by cutaneous passage through the rabbit (repeated transference from calf to calf being found to lead to deterioration).

Its potency is maintained for long periods if stored at 0°. Between 0° and 5° it may be expected to remain potent for three months, between 5° and 10° for four weeks only, and above 10° not more than seven days.

Glycerinated calf lymph has advantages over that obtained even from healthy children (as used in the past). The amount of protection afforded seems to be greater than that afforded by humanised lymph. Glycerinated lymph is recognised as the safest lymph for vaccination, and by the Vaccination Acts Amendment Act, 1898, it is enacted that if a child has not been vaccinated when 4 months and 1 week old, the public vaccinator of the district shall visit the home of the child, and shall offer to vaccinate the child with glycerinated calf lymph free of charge.

The Vaccination Order, 1929 (framed on the Report of the Rolleston Committee—*vide infra*) instructs public vaccinators to make single insertions of lymph instead of the previous 4 insertions, multiple insertions being available to those desiring them. Revaccination is to be encouraged at the ages of 5 to 7 and 14 to 16. In a covering letter, the importance of primary vaccination in infancy is emphasised, and as "post-vaccinal nervous disease" occurs mainly in children of school age or adolescents who have never been vaccinated, it is not considered wise to press for vaccination of such persons (unless directly exposed to infection) while the small-pox prevalent in this country retains its mild character. The new Order came into force on Oct. 1, 1929.

Chloroform water has been recommended to replace glycerin to kill off extraneous bacteria; more rapid effect. Urgent demands for vaccine, as in an epidemic, could be met by this method with a supply of vaccine in 14 days, instead of the month or 6 weeks necessary for glycerination.

Calf vaccine, diluted 10 to 50-fold with N/50 phosphate solution (pH 7.6) or with saline or sterile water, reduces risk of post-vaccinal encephalitis, and gives more satisfactory "takes."—S. P. Bedson, *Lancet*, ii/1929, 920.

**Post-vaccinal encephalitis.** On very rare occasions (8 cases were reported in this country in 1938) vaccination gives rise to a form of acute nervous disease which is frequently fatal. In the great majority of cases the condition arises following primary vaccination in adolescents or young adults, hence the Ministry of Health warning that primary vaccination at school age and in adolescents, except in special circumstances, is to be deprecated.

The exact nature of the agent responsible for the condition is undetermined. The special Committee set up by the Ministry of Health to consider the subject concluded that although no particular lymph can be incriminated, it is the vaccinia virus which initiates the nervous disturbance (see *Brit. med. J.*, i/1931, 64). On the other hand, the League of Nations Commission concluded that the virus of vaccinia itself is not responsible, but rather some unknown factor—a filter-passing or latent virus (see *Ser. L.o.N.P.*, 1928, iii, 12).

The incidence of post-vaccinal encephalitis is tending to fall in all the countries previously most affected, except Holland. Only 17,000 vaccinations were performed in Holland in 1935, the proportion of encephalitis cases being 1 per 1000 vaccinations.—per *Med. Annu.*, 1937, 541.

In none of 110 cases which had survived attacks of post-vaccinal encephalitis from two to six years earlier was there any serious impairment of health, and in particular there was noted the complete absence of the dreaded sequelæ of encephalitis lethargica, such as idiocy and epilepsy.—M. Kaiser and J. Zappert, *Munch. med. Wschr.*, 1937, 801.

For earlier references to post-vaccinal encephalitis see Vol. I 21st Edn.

**Chick Embryo Vaccine Lymph.** Experiments to provide a bacteria-free vaccine lymph led to the production by W. D. H. Stevenson and G. G. Butler of the Government Lymph Establishment of a lymph obtained by cultivation of the vaccinia virus on the chorio-allantoic membranes of chick embryos. Numerous clinical experiments have been made with this lymph, but it is too early yet to say whether there is any likelihood of it replacing calf lymph.

Dermal strain of vaccinia virus grown on the chorio-allantoic membrane of chick embryos. A possible large scale production of a bacteria-free virus. Experiments indicate that such a vaccine may be produced at little expense, absolutely free from contaminating micro-organisms and apparently producing on the rabbit lesions comparable to those produced by calf vaccine and, so far as observed, non-hæmorrhagic. The virus retains its potency at least two months in glycerin if kept below 0°C. Chicks usually hatch out from the inoculated eggs at maturity and healthy chicks result. Further effects on animals, especially monkeys, must be carefully watched.—W. D. H. Stevenson and G. G. Butler, *Lancet*, ii/1933, 228.

Satisfactory vaccination with chick embryo lymph, both with lymph of a sixth passage and of a 75th passage, in 7 persons. Appearances of vaccinia typical, and the reaction, if anything, milder than that produced by calf lymph. Way now cleared for trials on a wider scale. 38 eggs opened on the fourth day of their incubation after inoculation with vaccinia yielded sufficient lymph to vaccinate 7000 persons.—E. W. Goodpasture and G. J. Buddingh, *Science*, Nov. 24, 1933.

**Whooping Cough**

**Vaccinum Pertussis (B.P.C.).** *Syn.* PERTUSSIS VACCINE, WHOOPING COUGH VACCINE, BORDET-GENGOU BACILLUS VACCINE.

A simple sterile suspension of freshly isolated cultures of smooth phase I organisms of *Hæmophilus pertussis*, grown on Bordet-Gengou medium containing potato extract, glycerin and human blood. For details of *H. pertussis*, see Vol. II.

Is of service for active immunisation in non-epidemic times, for preventing the development of the disease in contacts, and for the treatment of symptoms; it reduces the violence and frequency of the paroxysms and shortens the duration of the attack.

Since the *Hæmophilus influenzae* (Pfeiffer) and the pneumococcus are frequently secondary invaders in whooping cough, the incorporation of these two organisms in vaccines used for treatment is likely to be beneficial. For prophylaxis, either a vaccine prepared from Bordet's bacillus (*H. pertussis*) alone, or a mixed vaccine containing the pneumococcus and Pfeiffer's bacillus also may be used. The simple Bordet's bacillus vaccine does not cause much reaction even in young infants, but care is necessary to avoid giving too large doses of pneumococcus and Pfeiffer's bacillus if the mixed vaccine is used.

A review of the literature during recent years shows conflicting views on the subject of dosage. For a number of years Sauer in America advocated a total of 80,000 million organisms, and Silverthorne in Canada has given a total of 120,000 million organisms. Smaller doses have been used in Great Britain, and the following recommendations are based on the experience of Maclean at St. Mary's Hospital, London.

*Dose.*—For prophylaxis, in non-epidemic periods, children may be given three doses each of 4000 million at intervals of 3 to 7 days, and a fourth dose of 4000 million not less than four weeks after the third dose.

In the case of contacts, as the maximum incubation period is fourteen days, the interval between the doses should be shortened so as to allow the development of as much immunity as possible within the incubation period; three doses of 4000 million each should be given at intervals of 2 to 3 days.

For treatment, children over 6 years of age should be given doses at intervals of 24 to 48 hours, commencing with 800 million and increasing by 400 million up to 4000 million. Children under 6 years should have half these doses. With these doses may be included appropriate amounts of *H. influenzae* (Pfeiffer) and pneumococcus.

The nature of the culture medium used for the preparation of the vaccine is of great importance in regard to antigenic capacity. Freshly isolated strains should be grown on media containing fresh human blood in order to retain the pathogenic phase I (see Vol. II).

There is no danger in vaccines for whooping cough, and after a reasonable initial dose enormous doses can be given with safety. To get results it is necessary to give at least 5 times the ordinary amount:—At 1 year a suggested second dose is 400 millions of ordinary, or 8000 millions of detoxicated vaccine, with maximum quantities of 1000 and 25,000 millions respectively. No case treated without definite benefit since using these large amounts.—R. W. Cockshut, *Brit. med. J.*, ii/1933, 819.

Controlled experiments with vaccine in the treatment of 60 children showed that the injection in the paroxysmal stage of large doses of a pertussis vaccine prepared in accordance with modern methods and beliefs neither curtails the duration of the disease nor ameliorates the symptoms.—N. D. Begg, *Lancet*, i/1936, 83.

The incubation period is probably 3 to 7 days, which is shorter than formerly supposed. By the cough-plate method it is possible with some degree of certainty to pronounce a patient free from infection after 3 weeks of illness. Freshly isolated organisms grown on human blood are necessary for the preparation of vaccines, and prophylactic vaccination with these organisms in doses from 30 to 80 billion at an early age is recommended. There is no evidence to show that vaccines are of any value in treatment, except possibly in the earliest stages. Convalescent human serum in doses varying from 20 to 40 ml., stated to be of value if given in the early catarrhal stage, and 10 ml. is probably an efficient prophylactic dose for contacts either before possible infection or in the incubation phase.—R. E. Smith, per *Quart. J. Med.*, 1936, 321.

Of 747 patients given a total of 120,000 million organisms, 91 exposures occurred, only one of whom contracted the disease. In 161 controls there were 27 exposures, 23 (85%) of whom contracted the disease.—Silverthorne and Fraser, *Canad. med. Ass. J.*, 1938, 556.

The consensus of opinion in this country is unfavourable to the use of vaccines in the treatment of whooping cough. When given in the paroxysmal stage they may even cause an increase in the frequency and severity of the spasms. Nevertheless, the use of small frequently repeated doses in the early stages should not be discouraged.—R. Cruickshank, *Lancet*, ii/1938, 33.

Investigation of a prophylactic vaccine containing 10,000 million smooth phase *H. pertussis* per ml. on 5815 children between the ages of 8 months to 4 years, the investigation extending over a consecutive period of 44 months. The vaccine was given subcutaneously in doses of 1 ml., 1.5 ml., and 3 ml. at weekly intervals. The final analysis was based on a test group of 1815 vaccinated children and 2397 controls. There were 15.1 per 100 annual pertussis attacks in the control group, compared with 2.3 per 100 in the vaccinated group, and there was a marked difference in the severity of the attacks in favour of the vaccinated group. After all known exposures the attack rate was 12.8 and 65.8% for the test and control groups respectively. By imposing the monthly incidence of pertussis (calculated on the experience of the experiment) on an imaginary section of the general population of 1000 injected children and a similar number of controls, at the end of 44 months 94.4% of the injected children would have escaped pertussis against 61% of the controls.—P. Kendrick and G. Elderling, *Amer. J. Hyg.*, 1939, 133.

211 infants vaccinated with vaccine prepared from unwashed phase I organisms; total dose 80,000 million. During 34 months there were 29 exposures with 9 cases of whooping cough. Among 182 controls in the same period there were 32 exposures and 29 cases of whooping cough.—Miller and Faber, *J. Amer. med. Ass.*, i/1939, 1145.

In a test group, 513 children received a total of 16,000 million organisms each; 46 of these were known to be subsequently exposed to whooping cough and 45 others were suspected exposures but no cases of whooping cough occurred. In a control group of 154 exposures 89 cases occurred.—I. H. Maclean, *Proc. R. Soc. Med.*, 1940, 33, 425.

**Formalinised vaccine** given intracutaneously or subcutaneously in total dosage of 30 billion organisms effective in prophylaxis.—Blatt, Levine and Shapiro, *J. Pediat.*, 1938, 12, 619.

**Sauer's Vaccine.** Prepared from hæmolytic strains of the Bordet-Gengou acillus, the culture medium containing 10% of defibrinated human blood. It contains 10,000 million bacilli per ml. *Dose.*—Children under 3, 8 ml. in divided doses, 1 ml., 1.5 ml., and 1.5 ml. under the skin of each arm, at weekly intervals. Children over 3, 1 ml., 2 ml., and 2 ml. respectively.—L. W. Sauer, 2nd Congress for Microbiology, London, 1936.



**Oral Whooping Cough Vaccine** (*Research Products, London*) contains per ml. *H. pertussis* 500 millions, *H. influenzae* (Pfeiffer) 250 millions, pneumococci 200 millions, *A. bronchitica* 50 millions. *Dose*.—For prevention: Age 10 to 16 years, 1 fl. oz. weekly; 7 to 10, 5 teaspoonfuls weekly; 2 to 7, 3 teaspoonfuls weekly; under 2, one teaspoonful weekly. For treatment, half the above dosage twice weekly. It should be administered upon an empty stomach, diluted with water.

**Pertussis Antigen (Detoxified)** (*Lederle Laboratories, New York; Thackray, Leeds*). A formalinised filtrate of the toxic principle derived from smooth phase I strains of *H. pertussis*; it is free from bacterial cells and contains a minimum of autolytic products. *Dose*.—*Curative*: 1.5 to 2 ml. subcutaneously every other day for 3 to 5 injections; *Prophylactic*: 3 subcutaneous injections of 2 ml. at weekly intervals; *Immunisation of direct contacts*: 3 subcutaneous injections of 1.5 to 2 ml. every 2 or 3 days.

**Pertussis U.B.A.** (*Lilly, London*). The undenatured bacterial antigen (see p. 1025) of *H. pertussis*. *Dose*.—*Curative*: 0.25 ml. subcutaneously, increasing by daily injections up to 1 to 1.5 ml. for 10 to 15 doses. *Prophylactic*: 1 ml. subcutaneously, followed every other day by 1.5 ml. until 6 doses have been injected.

Recently isolated strains of *H. pertussis* are grown on Bordet's medium enriched with human blood. The bacteria are washed in buffered isotonic solution and disrupted in a ball-mill. The suspension is filtered through acetic-collodion membranes and the antigen obtained as a water-clear filtrate.—J. W. Frawley, *J. Amer. med. Ass.*, ii/1934, 960.

A controlled study indicated that undenatured bacterial antigen conferred negligible immunity. A vaccine similar to Sauer's vaccine gave 83.4% protection of exposed children.—C. H. Singer-Brooks, *J. Pediat.*, 1939, 14, 25.

**Petein** (*Schering, London*). Detoxicated pertussis vaccine produced from 60 different strains of Bordet-Gengou organisms. Bottles of 2.5 ml. contain 50,000 million organisms. For the prophylaxis and treatment of whooping cough. Treatment consists of three injections over a week in consecutive doses of 0.5, 1.0 and 1.0 ml.

**Topagene** (*Sharp & Dohme, London*). A sterile solution of soluble antigenic substances from phase I culture of *H. pertussis* for the intranasal treatment of whooping cough. Each ml. represents the antigenic substances from 20,000 million organisms, a mercurial preservative in a dilution of 1 in 20,000 being added. 0.25 ml. is applied to the middle and superior turbinate area of each nostril once daily, or on alternate days for at least 2 weeks. Improvement should follow 4 to 5 applications, especially in early cases. Used prophylactically, the preparation will abort or markedly modify an attack.

**Convalescent Serum** from whooping-cough cases has been used with benefit in prophylaxis, but with doubtful benefit in treatment of pertussis. With Sauer's vaccine, immunity is completed in 4 months and lasts for years.—D. Paterson, R. H. Bailey, R. G. Waller, *Lancet*, ii/1935, 361.

## BLOOD TRANSFUSION

The recognition of blood groups, and the introduction of the indirect method of transfusion of citrated blood, by means of which clotting is avoided, has changed blood transfusion from a difficult and hazardous procedure, to be undertaken only in rare emergencies, to a safe and comparatively simple measure which is rapidly finding increasing use in a wide variety of conditions.

Thus, blood transfusion is currently employed following any type of severe hæmorrhage, such as post-partum hæmorrhage, traumatic hæmorrhage due to injury or war wounds, hæmatemesis, etc., in hæmorrhagic diseases, in severe shock, in subacute and chronic infections, and in pernicious anæmia and certain forms of secondary anæmia.

In the selection of a donor, an adult individual of either sex is suitable. The donor should be reasonably healthy and free from any disease transmissible by blood (syphilis and malaria in particular), and if possible allergic individuals should be excluded.

Since the bloods of different individuals, even of the same family, are not always compatible with each other, two such incompatibles cannot act as donor and recipient respectively, owing to the fact that incompatible bloods are liable to agglutinate or clump and to hæmolyse each other, causing serious reactions and even collapse. According to Moss (and Jansky) there are four distinct classes or groups of bloods. This means that the blood of a person in a particular group can safely be mixed with that of another person belonging to the same group, but not necessarily with the blood of a person belonging to one of the other groups.

Three systems of classification of the four groups have been suggested. The Moss classification is the one which has been most employed in this country, while the Jansky classification has been most used on the Continent, but in place of both of these the League of Nations Committee on Standardisation recommends the International Classification, which identifies the agglutinogens in the red blood cells, and is based on Landsteiner's Law of Iso-agglutinins.

According to Landsteiner, there are present in human blood corpuscles two agglutinable substances, A and B, which react with specific agglutinins (a) and (b) in serum. If any blood contains an agglutinable substance, it will contain the agglutinin which reacts with the alternative agglutinable substance. Thus, blood which contains the A substance will contain (b) agglutinin, and *vice versa*. The law is "In any blood there are always present agglutinins against the agglutinable substances absent from the same blood."

The relationship between these three systems is shown in the following table:

Moss	International	Jansky
I	AB	IV
II	A	II
III	B	III
IV	O	I

With samples of serum from the Groups A and B it is possible to test the blood of any donor before transfusion. The blood of Group AB does not cause agglutination of the cells of either of the other groups. Hence, these individuals are "universal recipients," because they can receive blood from each of the other three groups; they cannot, however, give blood to any but their own group. Since the corpuscles of Group O are not agglutinated by the serum of any other group, the members are "universal donors."

Wherever possible the donor should belong to the same group as the recipient, but where this cannot be arranged a donor of another compatible group may be used according to the following table:

Group	may receive from	may give to
AB	AB A B O	AB
A	A O	AB A
B	B O	AB B
O	O	AB A B O

**Technique of Blood Grouping.** Wherever the facilities are available, blood grouping should always be carried out by an expert. Standard test sera of Groups A (II) and B (III) are required, and these must be absolutely fresh (blood-grouping sera are now available commercially). The method of performing the test is to place a drop of each serum at either end of a glass slide, and to add to each a drop of normal saline and a drop of the blood to be tested (taken from the finger or ear). The mixtures are then stirred with a match-stick on the end of a glass slide, and the result observed. Agglutination is visible to the naked eye and appears as a deposit, the particles of which may get larger until in some cases a few crimson dots float in clear serum; for certainty, however, the reactions should be examined under the 2/3 objective.

Result observed	Group to which blood belongs
Agglutination with both sera .. ..	AB
No agglutination with either serum .. ..	O
Agglutination with Group B serum only ..	A
Agglutination with Group A serum only ..	B

Where it is not possible for the grouping to be done by an expert, or on occasions of great urgency when no known sera are available, a suitable donor may be selected by the *direct test*. A sample of serum is obtained from the recipient, by withdrawing 2 ml. of blood from a vein and allowing the serum to separate, and a sample of the corpuscles of each of the prospective donors is obtained by allowing two drops of blood from the finger or ear to fall into a small test-tube containing 2 ml. of normal saline, and mixing thoroughly. A drop of the recipient's serum is then placed on a clean glass slide or porcelain tile, and a drop of the cell suspension from the prospective donor is added to it, mixed with a match-stick, and gently rocked to and fro. If the prospective donor's cells are not agglutinated within 15 to 30 minutes, the donor may be regarded as suitable for the transfusion. To further ensure complete compatibility a drop of the recipient's blood may be mixed with a drop of the donor's serum and saline, and the result observed.

**Collection of Blood from Donor.** Both to the operator and the donor, the indirect use of citrated blood has definite advantages over the direct arm-to-arm technique with whole blood, and it is now the method almost universally employed.

For the collection of the blood the selected donor lies on a couch, with his arm extended away from the side and supported on a firm pad or pillow. A vein is selected at the elbow, the skin cleansed with spirit, and the sphygmomanometer adjusted to the arm, sufficient pressure being raised to cause the vein to stand out prominently. 1 or 2 m. of a 2% solution of procaine hydrochloride is then given over the site of the intended puncture, the injection being made with a fine needle, and a tiny nick is then made into the skin. To draw off the blood a French's needle is employed, to which is attached about 12 inches of wide-bore rubber tubing. The needle is inserted into the lumen of the distended vein through the small nick in the skin; before the needle is inserted both needle and rubber tubing should be washed through with citrate solution. The blood is received into a sterile graduated flask containing 3.8% sodium citrate solution (about 10 ml. for every 90 ml. of blood to be transfused), and the flask must be maintained at body heat by standing it in a basin of warm water. The blood is thoroughly mixed with the sodium citrate solution by continually rotating the flask or by stirring with a sterile glass rod. A steady flow of blood is maintained by adjustment of the sphygmomanometer and by the donor opening and closing his hand at regular intervals. As a rule about 500 ml. of blood is collected from one donor. The blood should be given to the recipient as soon as possible after collection, and it should be kept warm in the meantime, though care should be taken to see that it is not overheated.

The withdrawal of 500 ml. of blood seldom causes the donor any unpleasant feelings or reactions, but it is advisable that he

should lie down for half an hour after the collection and should be given some light refreshment before leaving.

**Transfusion into the patient.** The blood may be given to the patient either by means of (a) a single transfusion, or (b) by continuous drip transfusion. The former method is preferable where urgency is desired, or where hospital facilities are not available; the latter is essentially a hospital procedure, and has proved especially valuable in the treatment of anæmias.

(a) *Single transfusion.* When a vein is readily accessible the transfusion can be made by inserting the needle directly into it, the infusion apparatus being connected to the needle by an adaptor. But when, as often happens, the veins are collapsed or difficult to find, a suitable vein must be exposed and the needle inserted directly into it, employing a similar procedure as outlined above for collection of blood from donor, or the vessel is cut across, ligatured with catgut, and a cannula inserted; in this case care must be taken not to divide the vein completely—about half the circumference of the vein is adequate.

Various types of apparatus are employed for the infusion, that used for the funnel-gravitation method being the simplest and most inexpensive. This apparatus consists of a graduated glass funnel of some 300 ml. capacity, to which is attached about 2 feet of stout rubber tubing, into the end of which is inserted a metal nozzle to fit the needle. The cylinder and rubber tubing are first washed through with sodium citrate solution, and the funnel is then filled with blood, which is first filtered through layers of sterile gauze placed over the mouth of the funnel. The blood is allowed to flow slowly into the patient by gravity, the funnel being constantly replenished with blood, until the required amount has been given; the operator must keep the needle steady with his hand throughout the transfusion. The blood should not be transfused into the patient too rapidly; a single transfusion of from 500 to 600 ml. should take from 30 to 40 minutes. Care must be taken to see that the blood is kept warm. A small quantity of normal saline should precede and follow the transfusion.

(b) *Continuous drip transfusion.* This method is valuable for giving large amounts of blood over a continuous period, and is especially applicable in severe gastric or duodenal hæmorrhage, also in pre-operative cases in which there is severe anæmia. A satisfactory rate of flow is 40 drops per minute, i.e., a pint in 4 hours, and the total amount required is governed by the hæmoglobin figure; it is estimated that 750 ml. of blood will raise the hæmoglobin in an average adult about 15%. As with the single transfusion, the blood must be kept warm, and provision must be made to avoid the cells settling in the reservoir, either by shaking or stirring the contents, or by passing a continuous stream of oxygen through the blood.

(For a description of other methods of blood transfusion,

including the Jubé Syringe method and the Keyne's Flask method, see paper by H. F. Brewer, *Brit. med. J.*, i/1938, 241.)

The average in 87 cases treated by continuous drip transfusion was 5 pints and 29 hours, the largest figures being 11 pints and 62 hours. A pint is woefully inadequate for an anemic patient, especially if he is bleeding. The principle should be made one of quantitative measurement and the restoration of a normal hæmoglobin percentage. Hæmoglobin estimations should check the infusion. The best rate is to try to increase the patient's hæmoglobin by 10% every 4 hours, i.e., in the non-bleeding patient, a pint in 4 hours, or 40 drops a minute. In bleeding patients, the rate must be governed by hæmoglobin estimations. If the patient is weak there should be three stages at intervals of a few days. The method has proved extraordinarily effective. In peptic ulcer the blood can be run in as it is lost; 18 out of 22 serious cases had lived, and at least half of them could not have lived without the massive transfusion.—H. L. Marriott and A. Kekwick, *Lancet*, i/1936, 86; see also *Lancet*, i/1935, 977, and ii/1935, 78, for description of apparatus.

The following is a summary of the principles regarding the rate of transfusion in anemia uncomplicated by acute hæmorrhage: (1) The rate should never exceed 1 ml. per lb. bodyweight per hour; (2) In subjects suffering from very severe anemia, cachexia, or cardiac or respiratory disease the rate should not exceed 0.5 ml. per lb. bodyweight per hour; (3) The rate of flow should be maintained steadily and not accelerated even for short periods; (4) Careful watch should be kept for manifestations of cardiac failure (dyspnoea, cough, basal rales) and transfusion suspended if they appear. The custom of "giving a transfusion," meaning about a pint of blood in about half an hour, is irrational and unsatisfactory.—H. L. Marriott and A. Kekwick, *Brit. med. J.*, i/1940, 1043.

Blood transfusion for the practitioner—a simple domiciliary method.—G. R. Bashford, *Brit. med. J.*, i/1940, 901.

**Reactions.** Reactions resulting from blood transfusion may be due either to the too rapid administration of blood, to incompatibility of the blood, or to the presence of pyrogens or other bacterial by-products in contaminated blood.

Transfusions should always be made slowly; a too rapid administration may give rise to cardiac embarrassment, especially in debilitated patients.

Disturbances in which the patient becomes agitated, shivers and sweats, complains of severe lumbar pain, or shows signs of circulatory collapse, are due to faulty grouping; a further complication arising from this is hæmoglobinuria, due to hæmolysis of the transfused blood, and unless steps are taken at once to supply alkalis freely by the mouth, death may result from uræmia.

At the first signs of collapse, transfusion must be discontinued, and the patient given 5 minims of 1 in 1000 adrenaline solution.

Reaction following blood transfusion may be avoided by the use of a buffered citrate solution prepared as follows. *Stock solution.* Dissolve 0.6 g.  $\text{KH}_2\text{PO}_4$ , 0.9 g.  $\text{CaCl}_2$ , and 3.0 g. glucose in 100 ml. of distilled water. This keeps many months. *Buffered solution.* Take 30 ml. of physiological saline and 30 ml. of distilled water into a clean flask and add 2.0 g. of sodium citrate. Add 2 ml. of stock solution. Boil for 10 minutes. As the solution cools add a few drops of phenol red solution. The reaction will be alkaline. Filter while hot into another flask. When cool, 2 or 3 drops of normal HCl will give the copper colour of pH 7.3. Cover with a suitable rubber cap. This solution keeps indefinitely. For use take one volume of the solution for nine volumes of blood.—Temple Grey, *Lancet*, ii/1937, 1431.

Complete bacteriostasis of the usual bacterial contaminants in stored blood is made possible by the addition of 20 mg. per 100 ml. of sulphanilamide. Such blood will not only not support bacterial growth for 10 to 15 days, but may actually become sterile in that time.—M. Novak, *J. Amer. med. Ass.*, ii/1939, 2227.

**Stored blood in transfusion.** The increasing use of blood transfusion in current therapeutic practice and, more recently, the need for large and rapidly available supplies of blood for war emergencies, led to numerous laboratory and clinical investigations as to the value of stored blood for transfusion purposes. It has now been definitely established that blood may be satisfactorily preserved for periods up to 3 weeks by storing in an ice-box at 4°C. The blood is collected from donors in the usual way into pint bottles, each bottle being labelled with the donor's name, group, and date of bleeding, and the results of a sterility test and Wassermann reaction. Various types of anticoagulant diluent have been suggested, including both 2.5% and 3.8% sodium citrate solution, and what is known as I.H.T. solution, consisting of sodium chloride 7 g., sodium citrate 5 g., potassium chloride 0.2 g., magnesium sulphate 0.04 g., and distilled water to 1000 ml., and mixed volume for volume with the blood. The solution now advocated for use by the M.R.C. (see M.R.C. War Memo. No. 1, H.M.S.O., 1941) consists of 100 ml. of 3% sodium citrate in distilled water to which is added 20 ml. of 15% glucose in distilled water. The citrate and glucose must be of a high grade of purity and the distilled water filtered and autoclaved immediately after distillation. As glucose tends to caramelize during autoclaving in the presence of citrate the citrate and glucose solutions must be sterilised separately and mixed after sterilisation. 120 ml. of this anticoagulant solution is used for 420 ml. of blood.

Although stored blood may be used up to three weeks from the time of collection, the best results are obtained with blood not more than eight or ten days old. Stored blood should not be used for cases of traumatic shock uncomplicated by hæmorrhage.

During storage a certain amount of sedimentation occurs, and before use the flask is gently agitated to mix the cells again with the plasma.

It is essential that cross-matching should be done at the time of the transfusion, and when more than one lot of blood is given in one transfusion, each lot must be regrouped besides being cross-matched.

"Blood banks" have been established by numerous municipal and health authorities in various parts of the country for the storage and distribution of blood, and the Medical Research Council, on behalf of the Ministry of Health, has set up its own Emergency Blood Transfusion Depots in London and other large towns.

The following significant points should be stressed if optimum results in the use of stored blood are to be obtained: (1) The anticoagulant solution should be prepared from freshly distilled water from a clean still and should be filtered and autoclaved immediately. (2) All apparatus must be scrupulously clean. In the case of the rubber tubing a stiff wire, carrying a swab or narrow elongated brush, should be passed throughout its length, and new tubing must be washed to remove the French chalk with which its inside is coated. (3) Strict surgical asepsis should

be observed when collecting the blood. (4) Storage should be carried out at 2° to 4°C. (5) Blood showing undue hæmolytic should not be used. A zone of discoloration due to hæmolytic extending above the corpuscle layer up into the supernatant citrated plasma for  $\frac{1}{2}$  to 1 cm. or less may be allowed, but greater degrees, including complete tingeing of the plasma, should be a definite contra-indication to use. (6) Corpuscles and plasma may be mixed before the transfusion by as little and as gentle agitation as possible. (7) The blood should be warmed to body temperature before use; the avoidance of overheating is equally important. The highest temperature advised is 104°F.—H. F. Brewer, M. Maizels, J. O. Oliver and Janet Vaughan (M.O.'s in charge of Emergency Blood Transfusion Depots, set up by the M.R.C. on behalf of the Ministry of Health), *Brit. med. J.*, ii/1939, 1052.

For the treatment of anæmias, blood dyscrasias and infections, blood should not be used if it has been preserved for more than two or three days.—J. A. Kolmer, *Amer. J. med. Sci.*, April 1939.

Though stored blood is suitable for the treatment of acute hæmorrhage and shock, it is not advisable for use in cases of anæmia; fresh blood is preferred.—L. E. H. Whitby, *Practitioner*, ii/1939, 391.

As a result of 1458 transfusions of blood stored from one to 38 days it was found that no types of reaction were encountered distinctive of preserved blood, and the incidence of reactions did not increase or decrease with the period of storage of the blood mixtures. A limit of 10 days of storage at 3 to 5°C. was found to be safe for citrated blood, and blood stored in a dextrose-citrate mixture was found safe for transfusion after 30 days' storage.—E. L. DeGowin and R. C. Hardin, *Brit. med. J.*, ii/1940, 1.

From the standpoint of clinical results, stored blood is as good as fresh blood in acute hæmorrhage, and the available data present no evidence that it is of less value in non-acute hæmorrhage. On the average the gain in hæmoglobin is greater with fresh than with stored blood. Mild reactions occurred more commonly with stored than with fresh blood. There is an advantage in warming the blood to 37° before administration.—H. F. Brewer, M. Maizels, J. O. Oliver and J. Vaughan, *Brit. med. J.*, ii/1940, 48.

An account of the organisation of the Merseyside War Blood Bank. The blood taken is preserved in 3.8% sodium citrate, one pint to nine pints of blood. The unit adopted is one of 450 ml. (405 ml. of blood and 45 ml. of anticoagulant solution). 1364 transfusions with preserved blood have been given and the response to the administration of preserved blood in acute hæmorrhage and in chronic secondary anæmia is clinically satisfactory, and in these groups the ready availability of stored blood in bulk marks a true advance over the individual donor system. For certain other diseases of the hæmopoietic system, however, and for anæmia associated with sepsis, the administration of fresh blood is to be preferred. The incidence of all types of reaction is probably no greater with stored than with fresh blood, but it increases with the age of the blood, and it is recommended that stored blood should be administered if possible before it is ten days old.—F. R. Edwards and T. B. Davie, *Brit. med. J.*, ii/1940, 73.

**Changes in stored blood.** In blood stored in I.H.T. solution there is not only a decrease in the actual number of, but also degenerative changes in the remaining red blood cells. These changes may be seen two days after withdrawal and increase slowly during storage. All the white cells of the blood rapidly decrease in number, and at the end of a week the remaining nucleated cells are small lymphocytes. The fragility of the stored corpuscles to hypotonic saline begins to increase from the 8th to 9th day, while the sedimentation rate of the cells gradually diminishes, till by the 21st day of storage there is often no sedimentation. The appearance of stored blood, and particularly of the supernatant fluid, is not a true index of its transfusion value.—A. Macdonald and G. M. Stephen, *Lancet*, ii/1939, 1169.

Many of the solutions added to blood for the prevention of coagulation are hypertonic when compared with fresh erythrocytes. The mixture resulting from the addition is also hypertonic. The following solution is isotonic with fresh erythrocytes: sodium chloride 0.43%, sodium citrate 1.05%, and on experimental grounds should be preferred to other citrate solutions. The addition of dextrin to citrate-saline-blood mixtures enables storage to be continued for at least seven weeks, at the end of which time hæmolytic is less than half that observed in a simple citrate-saline-blood control.—M. Maizels and N. Whittaker, *Lancet*, ii/1939, 1219.



When fresh blood is mixed with a solution of 1.05% sodium citrate and 0.85% sodium chloride there is an initial decrease in volume, because the anticoagulant is hypertonic. Thereafter the cells lose their impermeability to salts, swell, and finally undergo hæmolysis. These changes may be checked and the blood preserved by the addition of dextrin.—M. Maizels and N. Whittaker, *Lancet*, i/1940, 113.

A suitable anticoagulant diluent for blood is sodium chloride 0.43%, sodium citrate 1.05%. It is, however, probably desirable to add glucose or dextrin in a final concentration of 1.0 and 3% respectively to improve preservation. If this is done the system becomes slightly more acid, and to counteract cell swelling due to acidity it may be desirable to increase the content of sodium chloride in the solution to 0.5%.—M. Maizels and N. Whittaker, *Lancet*, i/1940, 590.

Stored blood survives considerable periods after transfusion. Red cells stored for less than a week show about 70% of survival 14 days after transfusion. If storage is between 7 and 14 days, more than half the transfused red cells are still present in the recipient's circulation 14 days after transfusion. During storage normal cells lose potassium and take up a great excess of sodium. Within 24 hours of transfusion the chemistry of stored cells is restored to normal.—M. Maizels and J. H. Patterson, *Lancet*, ii/1940, 417.

A high proportion of the erythrocytes of stored blood survive transfusion. Furthermore, the total time of survival is little less than that of fresh blood.—P. L. Mollison and I. M. Young, *ibid.*, 421.

### Plasma and Serum Transfusions.

The use of stored blood for transfusion purposes, though an obvious advance on the use of fresh blood from the point of view of convenience, was found to possess certain disadvantages. Thus, it is limited in usage and source to the two most common groups O and A, from which the "blood banks" are made, and the necessity for correct blood grouping still remains; reactions are more common than with fresh blood, due in part to the increased potassium content and to increased fragility of the cells, especially in blood stored for more than 14 days.

Since the cells are one of the principal sources of reaction, attempts have recently been made to replace the use of whole blood by the use of either plasma or serum. Both possess the advantages that they may be kept indefinitely if stored in a cool dark place (they need not be kept in a refrigerator), and that they may be administered without preliminary grouping of the recipient and regardless of the group from which they have been collected.

Plasma and serum have identical therapeutic effects and are both excellent substitutes for whole blood for emergency purposes. They are particularly valuable in the treatment of shock (traumatic, post-hæmorrhagic or due to extensive burns) and in recent severe hæmorrhage. It should be emphasised, however, that when shock is associated with a degree of hæmorrhage sufficient to lower the hæmoglobin content by 50% or more, their use is contraindicated even as a temporary measure pending whole blood transfusion.

**Plasma** is the fluid content of whole blood, *i.e.*, whole blood minus the cells; it constitutes about 55% of the total volume, contains several important proteins and salts, and differs from whole blood chiefly in its inability to carry oxygen. It may be obtained either from stored or fresh blood, preferably from the latter, since that obtained from stored blood is almost devoid of bactericidal value and may have a high potassium content. The

chief disadvantage of plasma from the technical standpoint is the difficulty of filtration owing to the filter becoming choked with fibrin, and after storage for about a fortnight fibrin webs are apt to develop, necessitating further filtration before administration. Bottles of plasma which are uniformly turbid before shaking should not be used, since they are probably contaminated with bacteria.

**Serum** is the clear fluid expressed when blood clots (*i.e.*, plasma minus the substances which produce clotting) and may be obtained either from whole blood or from plasma (in the latter case by precipitating the fibrinogen by the addition of 8% calcium chloride solution and aspirating the serum from the clots formed—*see* J. W. Clegg and J. H. Dibble, *Lancet*, ii/1940, 294). It is preferably obtained from fresh blood or fresh plasma.

**Dried Plasma and Serum.** The difficulties encountered in connection with the storage and transport of large volumes of plasma and serum led to the production of these blood substitutes in desiccated form suitable for dissolving at the time of use (*see* F. R. Edwards *et al.*, *Brit. med. J.*, i/1940, 377, and F. X. Aylward *et al.*, *ibid.*, ii/1940, 583). The process of desiccation is one which needs skilled supervision and special apparatus and it is unsuited for undertaking by small-scale units.

The special advantages of the dried products are their stability, even at room temperature, their small bulk, and their high protein concentration. Their disadvantages are the loss of time entailed in getting them into solution and the difficulty in preserving sterility in solutions under emergency conditions.

For use, 20 g. of the dried product is dissolved in 500 ml. of 5% dextrose in sterile freshly distilled water. This has approximately the same concentration as citrated blood. They are employed similarly to whole blood. Dried plasma or serum after reconstitution should be used without delay and should not be stored away for future use.

A more recent development is the employment of concentrated solutions, *i.e.*, double or four times normal concentration. The drying of plasma and serum is carried out on a large scale at Cambridge, and the dried product is issued in 12 oz. bottles containing the solids from 200 ml. of plasma or serum. These are known as Cambridge "flats" and are marked at different levels, showing the volume of water required to bring the solution up to normal strength, or to twice or four times normal strength. The use of these concentrated solutions is still largely in the experimental stage and since they are highly viscous and often require to be given under pressure, they should be used with discretion pending further clinical investigation.

#### References to Use of Plasma and Serum.

Clinical reports on the use of stored blood and plasma include occasional unexplained reactions, and some of these may be due to the potassium content of the transfusion fluid, and it is wise, therefore, to use plasma with the minimum

potassium content until more precise information is available. It is recommended that separation of the plasma should be made as soon as possible after withdrawal of the blood, i.e., within two or three days.—B. R. G. Mainwaring *et al.*, *Lancet*, ii/1940, 385.

Under standard experimental conditions the therapeutic actions of various blood substitutes have been compared with whole blood and the conclusion is reached that plasma is the only one which, in the cat, consistently gives results approximating to those of whole blood. The other substitute solutions are placed in the following descending order of value: serum, hæmoglobin-Ringer, gum saline, red cells in crystalloid solution, isotonic saline, isotonic glucose. Filtration is the best method to overcome the danger of plasma infection.—G. A. H. Battle *et al.*, *Lancet*, ii/1940, 507.

**GASTRIC ULCER.** In patients suffering from severe hæmorrhage from the stomach or duodenum, plasma is not only of no value as a substitute for whole blood in therapy, but has given rise to untoward and dramatic ill-effects.—D. A. K. Black and A. F. Smith, *Brit. med. J.*, i/1941, 189.

**HÆMORRHAGE.** It is suggested that plasma transfusions should become a routine measure in the treatment of severe hæmorrhage.—H. J. Brennan, *Brit. med. J.*, i/1940, 1047.

**SHOCK.** In certain conditions transfusion of plasma is theoretically preferable to transfusion of whole blood. The over-concentration of the blood in shock, especially after burns, cannot very well be relieved by adding whole blood, and replacement of the lost fluid by plasma is a more rational method of treatment. If a supply of stored blood is available it is an easy matter to draw off the supernatant plasma. The red cells remaining behind can be resuspended in saline and transfused into anæmic patients who have no need of the plasma fraction.—Lehmann, *J. Amer. med. Ass.*, i/1939, 1406.

The preparation and use of dried blood plasma for transfusion. Its anti-shock property appears to be comparable to that of whole blood and it would seem ideal for use in emergency where no supply of blood is easily available, and in war surgery. 20 g. of dried plasma dissolved in 250 ml. of distilled water, or 500 ml. of 5% glucose in distilled water, is equivalent in plasma protein value to one pint of citrated blood.—F. R. Edwards *et al.*, *Brit. med. J.*, i/1940, 377.

In the treatment of post-hæmorrhagic shock, approximately 40% of the blood removed must be restored to secure recovery. Comparable volumes of serum or plasma produce equally satisfactory results. Experimental findings indicate: (1) that under these conditions the volume of the red cells restored to the animal is more important than their oxygen-carrying capacity; and (2) that serum and plasma, which can be stored for long periods, are effective blood substitutes for the treatment of hæmorrhage. It is important to administer blood or blood substitutes at a rapid rate (50 to 100 ml. per minute) as soon as possible after the hæmorrhage.—J. W. Magladery *et al.*, *Brit. med. J.*, ii/1940, 249.

The Treatment of Wound Shock:—Description of the Army Blood Transfusion Outfits and Instructions: Methods of Continuous Drip Blood Transfusion and Intravenous Infusion: The Reconstitution and Administration of Dried Serum or Plasma.—Committee on Traumatic Shock and on Blood Transfusion. *M.R.C. War Memo. No. 1*, H.M.S.O., 1941.

## POISONS

For the purpose of the *Pharmacy and Poisons Act, 1933*, and of the *Poisons Rules, 1935 to 1940*, a poison is any substance described in the *Poisons List*. The List is divided into two parts. Poisons included in the first part may be sold or supplied to the general public only by pharmacists; those in the second part by pharmacists and by persons whose names have been entered in a list by their local authority as defined by the Act. In either case the sale or supply may take place only from recognised premises and subject to the fulfilment of the conditions laid down in the Act and Rules.

Appended to the Poisons Rules are thirteen Schedules. Those of most general interest are *Schedules 1 and 4*. The former describes those poisons in respect to the sale, supply and storage of which more stringent conditions must be satisfied than are required for the other poisons in the Poisons List. The latter describes those poisons which may be sold to the public only upon the prescription of a doctor, dentist or veterinary surgeon. In *Schedule 3* are described articles which are exempted from the provisions of the Act and Rules. *Schedule 5* indicates the only form in which certain poisons named in Part II of the Poisons List may be sold by persons whose names have been entered in the local authority's list. *Schedule 7* describes those poisons the sale or supply of which, not being treated as a dispensed medicine (see page 1110), are, in the circumstances mentioned in the schedule, to be labelled with an indication of character other than the word "POISON." *Schedule 8* names those poisons which, except as medicines, may be transported only if certain conditions are fulfilled. The remaining schedules indicate those poisons which are exempted from the normal labelling provisions when sold or supplied in certain circumstances (*Schedule 2*); the manner in which the proportion of certain poisons may be calculated (*Schedule 6*); the form of application to be used by a person desiring his name to be entered in the local authority's list for the purpose of selling poisons in Part II of the Poisons List (*Schedule 9*); the form in which the local authority's list is to be maintained (*Schedule 10*); the form of the certificate for the purchase of a First Schedule poison to be used by a person not known to the seller (*Schedule 11*), the form of entry to be made in the Poisons Book when a First Schedule poison is sold (*Schedule 12*), and the form of authority for the purchase of strychnine for the purpose of killing moles (*Schedule 13*).

The Poisons List is set out in full on pages 1118 to 1119; the Schedules to the Poisons Rules on pages 1120 to 1128.

Throughout these notes no reference is made to poisons which are subject to the Dangerous Drugs Acts and Regulations, and in any transaction in respect of a "dangerous drug" the requirements of the Dangerous Drugs Acts and Regulations must be complied with in addition to the requirements summarised below. The words "doctor," "dentist," "veterinary surgeon," "pharmacist" and "wholesaler" mean, respectively, duly qualified medical practitioner (*i.e.*, registered in Great Britain under the Medical Acts); registered dentist; registered veterinary surgeon; registered chemist and druggist or pharmaceutical chemist; and a person, firm or body corporate who sells an article otherwise than to the general public. Where reference is made to poisons in the First Schedule only, such references do not apply to machine-spread plasters, surgical dressings, articles containing barium carbonate and prepared for the destruction of rats and mice, and corn paints in which the only poison is a

poison included in the Poisons List under the heading of "Cannabis."

### **General Prohibitions.**

(a) In no circumstances may a poison be sold or supplied by means of an *automatic machine*.

(b) *Strychnine*, otherwise than as an ingredient of a medicine, may not be sold or supplied except to (i) persons who require it to sell again; (ii) purchasers outside the United Kingdom to whom it is to be exported; (iii) persons requiring it for dispensing, and, if a doctor or veterinary surgeon, also for administration by himself or under his supervision; (iv) persons concerned with scientific education, research or chemical analysis, and requiring it for that purpose, and (v) persons who require it for the purpose of killing moles, provided they produce a written authority as set out in Schedule 13 (*see p. 1128*) not more than three months old, and signed by the executive officer or secretary of a County War Agricultural Executive Committee in England, or by the chairman or secretary of an Agricultural Executive Committee in Scotland; this authority must specify the amount of strychnine, not greater than four ounces, which the authorised person may buy, and must be retained by the seller.

## **HOW TO OBTAIN POISONS FOR USE IN "BUSINESS OR PROFESSION"**

A person "carrying on a business in which poisons are regularly sold or used in the manufacture of other articles" may purchase poisons from a manufacturer or wholesaler without formality. The seller, nevertheless, is required to satisfy himself that the purchaser of a First Schedule poison requires it for the purpose of his business or profession. Any other person (including organisations, hospitals or nursing homes) requiring poisons for use in his business or profession may purchase them from a wholesaler or a retailer. It will be observed that purchases may be made not only by those persons whose business or profession is directly concerned with medication, but also by others such as analysts, science teachers, research workers, and by persons such as farmers or market gardeners who use the poison in connection with agriculture or horticulture. If the poison is included in the First Schedule to the Poisons Rules, the purchaser must attend at the premises of the seller and sign the Poisons Book and supply the information necessary to enable the seller to make the required entries in that book (*see page 1111*).

Alternatively, the purchaser may order the poison from the seller by post or otherwise, provided that if the poison is included in the First Schedule the order must be in writing, signed by the purchaser, state his name and address, his business or profession, the name and quantity of the article to be purchased, and the purpose for which it is required. It is not necessary to state

business or profession or the purpose for which the poison is required when the purchaser is a hospital, infirmary, dispensary or clinic, or the purpose for which the poison is required when the purchaser is a doctor, dentist or veterinary surgeon.

Before supplying a First Schedule poison stated to be required for the purpose of the purchaser's business or profession, the seller must satisfy himself (a) that the poison is used in the business or profession of the purchaser; (b) that the purchaser is engaged in the business or profession stated, and (c) if the order is in writing, that the signature of the purchaser is genuine.

### **Emergency.**

In an emergency, a person who represents that he urgently requires a First Schedule poison for the purpose of his business or profession may be supplied if the seller is satisfied as to the emergency, and the purchaser at the time undertakes within 24 hours to attend personally and sign the entry of supply in the Poisons Book kept by the supplier or to furnish a written order as above. Failure on the part of the purchaser to fulfil such an undertaking is an offence.

## **THE SALE OR SUPPLY OF POISONS**

### **A. The doctor, dentist or veterinary surgeon.**

Doctors, dentists and veterinary surgeons may not sell or supply poisons except as medicines for patients under their care. If the supply is otherwise than by administration by the doctor, etc., personally, a record must be made in a book showing the date of supply, the ingredients and quantity of the medicine and the name of the patient. No record is necessary of the supply by a doctor (but not a dentist or veterinary surgeon) if the poison is not in the First Schedule, or if the medicine is supplied on a National Health Insurance prescription or on a prescription issued in connection with the health scheme of a local authority. Records where required must be made on the day on which the medicine is supplied or, if that is not reasonably practicable, on the following day. The container in which the medicine is supplied must be impervious to the poison and strong enough to prevent leakage from the ordinary risk of handling. The medicine must be distinctly labelled with the name and address of the practitioner, and if it is a liquid for external application, with the words "For external use only," together with the name of the article, e.g., "The Liniment," "The Lotion," "The Embrocation."

It is appropriate here to mention that a prescription given to his patient by a doctor, etc., for a medicine which is a poison in the Fourth Schedule to the Rules to be dispensed by a pharmacist otherwise than at a hospital must include the following particulars:-

- (i) the name and address of the person to whom the medicine is to be supplied, or, in the case of a prescription of a veterinary surgeon, the name and address of the person to whom the medicine is to be delivered;
- (ii) the date (to be inserted by the prescriber);
- (iii) the total amount of medicine to be supplied and the dose to be taken;
- (iv) the usual signature of the prescriber (not his initials);
- (v) the address of the prescriber (except in the case of National Health Insurance or Local Authority prescriptions);
- (vi) if to be repeated indefinitely or for a limited number of times, bear a statement to that effect;
- (vii) if the prescriber is a dentist, bear the words "For dental treatment only," and if a veterinary surgeon the words "For animal treatment only."

Doctors and others should note that unless the prescription contains the particulars indicated above, the pharmacist is not permitted to supply the medicine. Further, unless otherwise directed on the prescription he may not supply the medicine on more than one occasion. The pharmacist must also retain the prescription when it is no longer valid for further supply.

SPECIMEN FORM OF PRESCRIPTION FOR FOURTH SCHEDULE  
POISONS.1. *Doctor.*[Address of  
prescriber.]\*[Name and address of  
patient.][Name and quantity of ingre-  
dients, including dose and  
total amount of finished  
product to be supplied.]

[To be repeated X times.]†

[Date (to be inserted  
by prescriber).][Signature (not initials)  
of prescriber.]2. *Dentist.*

As above, but in addition the words "For dental treatment only" must be written on the prescription.

3. *Veterinary Surgeon.*

As for a doctor's prescription except that "the name and address of the person to whom the medicine is to be delivered" must be inserted in place of "the name and address of patient," and the words "For animal treatment only" must be written on the prescription.

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\*Address of doctor is not necessary in the case of National Health Insurance and Local Authority prescriptions.

†If not to be repeated, this entry should be omitted. If to be repeated indefinitely the statement should make it clear that such is the intention of the prescriber. If to be repeated on a limited number of occasions, the number should be clearly stated. If desired, the prescriber may state the actual dates upon which the medicine may be repeated; he may also indicate what period of time should elapse before repeating on any occasion.

**B. The pharmacist.**

Poisons may be sold or supplied to the general public by the pharmacist only from premises registered under Part I of the Pharmacy and Poisons Act, 1933, and only if he or his employer is an "authorised seller of poisons" within the meaning of that Act and the conditions set out below are fulfilled.

**I. Dispensing medicines on prescription of doctor, dentist or veterinary surgeon.****(A) Schedule 4 Poisons.**

The prescription must contain the particulars set out on page 1108.

The medicine must not be supplied more than once unless the prescriber has directed otherwise, in which case it may be supplied only in accordance with the directions. For example, if a prescription is marked by the prescriber "To be repeated X times" it may not be repeated more than X times; if "To be repeated" it may be repeated indefinitely.

The pharmacist must

- (i) mark on the prescription, above the signature of the prescriber, the date on which it was dispensed and the name and address of the seller;
- (ii) when the prescription is no longer valid to be dispensed again, retain it for two years;
- (iii) enter in the prescription book on the day the prescription is dispensed, or on the following day, the following particulars:—
  - (a) the date of supply,
  - (b) the name and address of the person to whom the medicine is supplied,
  - (c) the ingredients and quantity of the medicine,
  - (d) the name or initials and, if known, the address of the prescriber,
  - (e) the date on which the prescription was given.

When the medicine is repeated, the entry in the prescription book must show the quantity of medicine supplied and a reference to the original entry.

N.H.L. prescriptions need not be copied, but should be forwarded in the ordinary way for pricing.

Local Authority prescriptions must be copied unless, in addition to the prescription, a carbon copy is supplied to the pharmacist and retained by him;

- (iv) place the medicine in a container which is impervious to the poison and strong enough to prevent leakage from the ordinary risk of handling and transport. It will be noted that there is no obligation upon the pharmacist to put any 'dispensed' medicine in a 'poison' bottle (fluted vertically with ribs or grooves). This does not prevent him doing so, however, if he considers such course desirable.
- (v) label with the name of the seller and the address of the premises on which the medicine is sold, and if the medicine is a liquid for external application, with the words "For external use only" and the name of the article, e.g., Embrocation, Liniment, etc.

**(B) Poisons not included in the Fourth Schedule.**

The requirements set out under (iii), (iv) and (v) above for Schedule 4 poisons must be fulfilled, except that if the prescription is given by a doctor (but not a dentist or veterinary surgeon), and is not a First Schedule poison, no entry need be made in the prescription book.

**II. Dispensing medicine "counter prescribed" by pharmacist or to purchaser's own formula.****(A) Schedule 4 Poisons.**

In no circumstances may Fourth Schedule poisons be sold or supplied to the general public as a "counter prescribed" medicine or to the purchaser's own formula. A prescription from a doctor, dentist or veterinary surgeon is essential (see page 1109).

**(B) Poisons not included in the Fourth Schedule.**

The pharmacist must

- (i) enter in the prescription book on the day the prescription is dispensed, or on the following day, the following particulars:—



- (a) the date of supply,
- (b) the name of the person to whom the medicine is supplied,
- (c) the ingredients and quantity of the medicine. If the medicine is repeated, it is sufficient when repeating the entry in the prescription book to state the quantity of the medicine supplied and a reference to the original entry;
- (ii) place the medicine in a container which is impervious to the poison and strong enough to prevent leakage from the ordinary risk of handling and transport. It will be noted that there is no obligation upon the pharmacist to put any 'dispensed' medicine in a 'poison' bottle (fluted vertically with ribs or grooves). This does not prevent him doing so, however, if he considers such course desirable.
- (iii) Label with the name of the seller and the address of the premises on which the medicine is sold, and if the poison is a liquid for external application, with the words "For external use only" and the name of the article, e.g., Embrocation, Liniment, etc.

### III. Sales "over the counter."

#### (A) Schedule 4 Poisons.

In no circumstances may Fourth Schedule poisons be sold to the general public "over the counter." A prescription from a doctor, dentist or veterinary surgeon is essential (see page 1109).

#### (B) Poisons included in the First Schedule but not in the Fourth Schedule.

The pharmacist must

- (i) know the purchaser to be a person to whom the poison may properly be sold, or receive from the purchaser a certificate in the form prescribed in the Eleventh Schedule given by either
  - (a) a householder known to the pharmacist as a responsible person of good character, or
  - (b) a householder, and endorsed by a police officer in charge of a police station.

The certificate must be retained by the pharmacist;

- (ii) enter in the Poisons Book (which must be kept for at least two years after the date of the last entry) the following particulars:—
  - (a) the date of the sale;
  - (b) the name, address and business, trade or occupation of the purchaser;
  - (c) the name and quantity of the poison;
  - (d) the purpose for which the poison is stated to be required;
  - (e) if a certificate is supplied by the purchaser, the name and address of the person giving the certificate and the date on which the certificate was given;
- (iii) require the purchaser to sign the entry. Where the purchaser requires the poison for the purpose of his business or profession (see page 1107), it is not necessary for the purchaser to sign the entry if he supplies an order in writing giving the particulars set out on page 1107, in which case the pharmacist must enter the words "signed order" in the space provided for the purchaser's signature and a reference number to identify the order. This number must also be placed on the order by the pharmacist. The order must be kept for two years. If the poison is sent by post to a person purchasing it for the purpose of his business or profession it must be sent by registered post;
- (iv) label the poison with the particulars set out below. These must appear clearly and be in a conspicuous position on the actual container of the substance and on each covering, if any, of the container except transparent covering, or covering used solely for the purpose of transport or delivery. Where the poison is contained in an ampoule, cachet or similar article, it is not necessary to label the article itself if every covering in which the article is enclosed is duly labelled.
  - (a) the name of the seller and the address of the premises on which the poison is sold;

- (b) the name of the poison. If the term used in the Poisons List describes the poison specifically, the said term may be used. If the poison is a substance described in a monograph in the *B.P.* or *B.P.C.*, or a preparation contained in the *B.P.* or *B.P.C.*, whether concentrated, diluted or mixed with any other substance or not, or a surgical dressing described with standards in the *B.P.C.*, it is sufficient to use the official name, synonym or abbreviated name followed by the letters *B.P.* or *B.P.C.*, as the case may be. In any other case the accepted scientific name or the name descriptive of the true nature or origin of the poison must be used. For preparations containing a poison specified in the first column of the Sixth Schedule, the corresponding name of the poison contained in the second column may be used. In the case of preparations of nux vomica or opium, it is sufficient to use the names strychnine or morphine or one of the official names or abbreviated names of strychnine or morphine as set out at the head of the monographs in the *B.P.* or *B.P.C.*
- (c) the proportion of poison present if mixed with other ingredients in a preparation. This is not necessary if the poison is a substance, preparation or surgical dressing described in the *B.P.* or *B.P.C.*. If the poison is specified in the first column of the Sixth Schedule, the corresponding particulars stated in the second column should be used. If the statement of proportion is given as a percentage it must also state whether the percentage is weight in weight *w/w*, weight in volume *w/v*, or volume in volume *v/v*. For tablets, pills, cachets, capsules, lozenges, and similar articles, or ampoules, the quantity of poison in each and the number of articles may be stated. If the poison is contained in a *B.P.* or *B.P.C.* substance or preparation which is concentrated, diluted or mixed with any other substance, the proportion of the substance or preparation to the total product may be stated;
- (d) the word "Poison," or if the poison is allylisopropylacetylurea (*e.g.*, the proprietary article "Sedormid") or beta-aminoisopropylbenzene (*i.e.*, amphetamine) or phenylethylhydantoin (*e.g.*, the proprietary article "Nirvanol"), and is made up ready for the internal treatment of human ailments, the words "Caution. It is dangerous to take this preparation except under medical supervision." The required word or words must (i) be in red or on a red background, (ii) appear either on a separate label or within a line containing no words other than the particulars with which the substance is required to be labelled by the Act or Rules, and (iii) not be modified in meaning by other words or marks;
- (e) the words "For external use only" and the name of the substance (*e.g.*, The Embrocation, The Liniment, The Lotion, etc.) in the case of liquid medicines for external application. Mouth-washes, eye-drops, eye-lotions, ear-drops, douches and similar preparations are *not* regarded as medicines for external application for the purpose of this provision;
- (f) the words "Not to be taken" in the case of a liquid other than a medicine contained in a bottle of a capacity of 120 fluid ounces or less;
- (g) If the poison is compressed hydrocyanic acid, the container must be labelled with the words "Warning. This container holds poisonous gas, and should only be opened and used by persons having expert knowledge of the precautions to be taken in its use." If the poison is an arsenate, arsenite, copper acetoarsenite, halide of arsenic, organic compound of arsenic, oxide of arsenic, sodium thioarsenate, or sulphide of arsenic, and is intended for use in agriculture or horticulture for the destruction of bacteria, fungi, insects, vermin, or as weed-killer, it must be coloured with a distinctive water-soluble dye. This does not apply to lead arsenate paste or powder, poisons and sheep-dips which are themselves distinctively coloured, or articles to be exported to purchasers outside the United Kingdom.

(v) place the substance in a container which is

- (a) impervious to the poison and strong enough to prevent leakage from the ordinary risk of handling, and
- (b) fluted vertically with ribs or grooves if the substance is a liquid supplied in a glass bottle of a capacity of 120 fluid ounces or less, and is not a medicine made up ready for the internal treatment of human ailments, or a local anæsthetic for injection in the treatment of human or animal ailments. Mouth-washes, eye-drops, eye-lotions, ear-drops, douches and similar articles are regarded as medicines for external use for the purpose of this provision.

(C) *Poisons not included in either the First or Fourth Schedules.*

The pharmacist must

(i) label the poison with

- a) (i) the word "Poison" in the case of non-medicines, or medicines for external use (including mouth-washes, etc., as under (v) (b) above) or medicines for the internal treatment of human ailments not made up ready to be taken, or (ii) the words "Caution. It is dangerous to exceed the stated dose" in the case of medicines (other than those referred to under (iii) below) which are made up ready for the internal treatment of human ailments, or (iii) the words "Caution. It is dangerous to take this preparation except under medical supervision" in the case of insulin, the active principles of pituitary gland, and the active principles of thyroid gland and their salts, if made up ready for the internal treatment of human ailments. The required word or words must appear either on a separate label or within a line containing no words other than the particulars with which the substance is required to be labelled by the Act or Rules, and must not be modified in meaning by other words or marks;
- (b) the particulars set out under B (iv) (a), (b), (c), (e) and (f) above (page 1111), except that the name and address (see (a)) need only appear on the outer cover of the article.

(ii) place the poison in a container as set out under (B) (v) above.

#### IV. *Sales of poisons for use in business or profession.*

(A) *Schedule 4 Poisons.*

There are no special conditions which apply to the pharmacist in the sale or supply of Fourth Schedule poisons to a person requiring the poison for the purpose of his business or profession. All poisons in the Fourth Schedule are, however, First Schedule poisons, and the normal requirements which apply to such poisons and described in the next paragraph must be observed.

(B) *Poisons included in the First Schedule.*

The purchaser must either attend in person to obtain the poison, or supply an order in writing signed by himself stating his name and address, his business or profession, the name and quantity of the article to be purchased and the purpose for which it is required. It is not necessary to state business or profession or the purpose for which the poison is required when the purchaser is a hospital, infirmary, dispensary or clinic, or the purpose for which the poison is required when the purchaser is a doctor, dentist or veterinary surgeon.

The pharmacist must

(i) satisfy himself

- (a) that the poison is used in the business or profession of the purchaser, and
- (b) that the purchaser is engaged in the business or profession stated, and
- (c) if the purchaser does not attend in person, but supplies a written order, that the signature of the purchaser is genuine;

(ii) comply with the conditions set out under III B above (pages 1111 to 1113). In sales or supplies to a person or institution concerned with scientific education or research or chemical analysis, for the purposes of that education, research or analysis, the only requirement in regard to container is that it shall be impervious to the poison and strong enough to prevent leakage from the ordinary risk of handling.

See also note on Emergency (page 1108).

*(C) Poisons not included in the First Schedule.*

The pharmacist must comply with the conditions set out under **B III (C)** (page 1113).

**C. The wholesaler.**

Subject to the proviso that a person who is carrying on a business which comprises the manufacture of medicines for the treatment of animals, and who has complied with the requirements of Rule 4 of the Poisons Rules, 1935, may sell or supply a poison as a medicine for the treatment of animals, a wholesaler may not sell or supply any poison direct to the public unless he is *either*

- (a) an authorised seller of poisons, in which case he must comply with the requirements set out in this summary under Section **B—The pharmacist** (page 1110).
- or (b) a listed seller of poisons, in which case he may sell only certain poisons and must comply with the requirements affecting transactions by such persons. The requirements to be fulfilled by listed sellers of poisons are not set out in this summary.

Subject to the general prohibitions mentioned on page 1107 any wholesaler who is not carrying on a retail business on the same premises may sell poisons as set out under sections **I to IV** below; transactions referred to under sections **V to IX** below may only be effected if in addition the wholesaler regularly sells poisons to purchasers who require them either to sell again or to use in their trade or business.

**I. To a purchaser (either wholesaler or retailer) who buys for the purpose of selling again.***(A) Poisons included in the First Schedule.*

The wholesaler must

- (i) be satisfied that the purchaser requires the poison for the purpose of selling again;
- (ii) comply with the requirements set out under **B III (B)** (iv) and (v) (pages 1111 to 1113), subject to the proviso that no name and address is necessary if the poison is to be sold again in the same container, and the requirements of **B III (B)** (iv) (b) to (d) need not be satisfied if the poison is included in the Second Schedule, is sold to a wholesaler who carries on a business in the course of which poisons are either regularly sold to purchasers who buy to sell again or regularly used in the manufacture of other articles, and who requires the poison for the purpose of that business, is labelled with the name of the seller and the address of the premises on which it is sold, and the outside of the package is labelled conspicuously with words indicating the dangerous properties of the poison.

*(B) Poisons not included in the First Schedule.*

The wholesaler must comply with the requirements set out under **B III (C)** (i) and (ii) (page 1113), subject to the proviso that no name and address is necessary if the poison is to be sold again in the same container, and the requirements of **B III (C)** (i) (a) and **B III (B)** (iv) (a) to (c) need not be satisfied if the poison is included in the Second Schedule, is sold to a wholesaler who carries on a business in the course of which poisons are either regularly sold to purchasers who buy to sell again or regularly used in the manufacture of other articles, and who requires the poison for the purpose of that business, is labelled with the name of the seller and the address of the premises on which it is sold, and the outside of the package is labelled conspicuously with words indicating the dangerous properties of the poison.

**II. To be exported to purchasers outside the United Kingdom.**

The requirements for all poisons, whether or not First Schedule, are the same; the wholesaler must comply with the requirements set out under **B III (B)** (v) (a) (page 1113).

It will be noted that for export there are no requirements prescribed for labelling poisons, other than those for transport. Sales to Northern Ireland are not export sales, but such sales are exempt from the labelling requirements as set out under **B III (B)** (iv) (pages 1111 to 1112) and **B III (C)** (i) (page 1113), if the poisons are labelled in accordance with the laws of Northern Ireland.

**III. To a doctor, dentist, or veterinary surgeon for the purpose of their respective professions.**

The wholesaler must comply with the requirements as set out under **B IV** (page 1113).

**IV. For use in or in connection with any hospital, infirmary, dispensary or similar institution approved by order, whether general or special, of the Secretary of State.**

(By the Poisons (Approved Institutions) Order, 1935, the Secretary of State has approved any hospital, infirmary or dispensary maintained by any public authority or out of any public funds, or by a charity or by voluntary subscriptions.)

The wholesaler must comply with the requirements as set out under **B IV** (page 1113).

**V. To a person who requires the poison for the purpose of his trade or business.**

**(A) Poisons included in the First Schedule.**

The wholesaler must

- (i) be satisfied that the purchaser requires the poison for the purpose of his trade or business;
- (ii) comply with the requirements set out under **B III (B)** (iv) and (v) (pages 1111 to 1113); except that

(a) if the poison is included in the Second Schedule, is sold to a wholesaler who carries on a business in the course of which poisons are either regularly sold to purchasers who buy to sell again or regularly used in the manufacture of other articles, and who requires the poison for the purpose of that business, is labelled with the name of the seller and the address of the premises on which it is sold, the requirements of **B III (B)** (iv) (b) to (f) need not be satisfied, provided the outside of the package is labelled conspicuously with words indicating the dangerous properties of the poison;

(b) if sold to a person concerned with chemical analysis a fluted bottle need not be used.

**(B) Poisons not included in the First Schedule.**

The wholesaler must comply with the conditions set out under **B III (C)** (page 1113), except that

- (a) if the poison is included in the Second Schedule, is sold to a wholesaler who carries on a business in the course of which poisons are either regularly sold to purchasers who buy to sell again or regularly used in the manufacture of other articles and who requires the poison for the purpose of that business, the requirements of **B III (C)** (i) need not be satisfied, provided the requirements of **B III (B)** (iv) (a) are satisfied, and the outside of the package is labelled conspicuously with words indicating the dangerous properties of the poison;
- (b) if sold to a person concerned with chemical analysis a fluted bottle need not be used.

**VI. To a person who requires the poison for the purpose of enabling him to comply with any statutory requirements in respect of the medical treatment of his employees.**

The wholesaler must comply with the statutory requirements as set out under **B IV** (page 1113).

**VII. To a Government department or an officer of the Crown requiring the poison for the purposes of the public service.**

The wholesaler must comply with the requirements as set out under **B IV** (page 1113).

**VIII. To a local authority requiring the poison in connection with the exercise of statutory powers.**

The wholesaler must comply with the requirements as set out under **B IV** (page 1113).

**IX. To a person or institution concerned with scientific education or research if the poison is required for the purpose of that education or research.**

The wholesaler must comply with the requirements as set out under **B IV** (page 1113), except that in no circumstances is it necessary to use a fluted bottle.

**D. Hospitals and similar institutions.**

**I. Out-patients.**

The ordinary rules governing the supply of poisons do not apply to any poison which is a medicine supplied for the treatment of human ailments from a hospital, infirmary or dispensary maintained by any public authority, or out of any public funds, or by a charity, or from any institution approved by the Minister of Health for the purpose of section 24 (4) of the National Health Insurance Act, 1924, or for the treatment of animals from a veterinary hospital which is under the superintendence of a veterinary surgeon, if the conditions set out below are satisfied.

(It will be noted that this does not authorise the *sale* of poisons. "Sales" may only be effected if the institution becomes an authorised seller of poison within the meaning of the Pharmacy and Poisons Act, 1933.)

- (a) the medicine must not be supplied except by or on and in accordance with a prescription of a doctor, for the purposes of medical treatment, or a dentist for the purposes of dental treatment or a veterinary surgeon for the purposes of animal treatment;
- (b) if a First Schedule poison, a record must be kept on the premises so that at any time during the two years following the supply there can readily be traced the following particulars:—
  - (i) the name and quantity of the poison supplied;
  - (ii) the date of supply;
  - (iii) the name and address of the person supplied;
  - (iv) the name of the person who supplied the poison or who gave the prescription upon which it was supplied.

These requirements need not be satisfied in the case of a National Health Insurance prescription.

- (c) The container of the medicine must be labelled
  - (i) with a designation and address sufficient to identify the hospital or other institution from which it was supplied;
  - (ii) with the word "Poison" except in the case of a medicine made up ready for treatment;
  - (iii) with the words "For external use only" and the name of the article, e.g., The Embrocation, The Liniment, etc., if the poison is a liquid for external application;
  - (iv) with the words "For animal treatment only" if the poison is supplied from a veterinary hospital;

**II. In-patients.**

In any hospital, infirmary, dispensary, clinic, nursing-home, or other institution at which human ailments are treated, and in which medicines are dispensed in a separate dispensing or pharmaceutical department in charge of a person appointed for that purpose, no medicine containing a poison must be supplied from that department (except in cases of emergency) for use in the wards, operating theatres, or other sections of the institution unless

- (a) a written order signed by a doctor, dentist, or by a sister or nurse in charge of a ward, theatre or other section of the institution, is received; and
- (b) the container is labelled
  - (i) with words describing its contents;
  - (ii) in the case of First Schedule poisons with a distinguishing mark or other indication, indicating that the poison is to be stored in a cupboard reserved solely for the storage of poisons.

**STORAGE OF POISONS**

**A. The doctor, dentist or veterinary surgeon.**

There are no regulations affecting the storage of poisons in the surgery of a doctor, dentist, or veterinary surgeon.

**B. The pharmacist.**

With the exception of the general requirement that the container shall be impervious to the poison and stout enough to prevent leakage from ordinary risks of handling, only First Schedule poisons are affected by the provisions governing storage. Such poisons must be stored in manner set out below (but all three systems may be in use at the same time, and for the same substance):

- (i) in a cupboard or drawer reserved solely for the storage of poisons; or
- (ii) in a part of the premises which is partitioned off or otherwise separated from the remainder of the premises, and to which the public have not access; or
- (iii) on a shelf reserved solely for the storage of poisons; provided that
  - (a) no food is kept beneath the shelf; and
  - (b) the container of the poison is rendered distinguishable by touch from the containers of articles and substances other than poisons stored upon the same premises.

First Schedule poisons for use in agriculture or horticulture must be stored only in a cupboard or drawer reserved solely for such poisons or in accordance with (ii) above, provided that food is not kept in that part of the premises.

**C. The wholesaler, educational institutions and laboratories.**

There are no restrictions affecting the storage of poisons by wholesalers, educational institutions and laboratories, other than the general requirement that the container of the poison shall be impervious to the poison and stout enough to prevent leakage from the ordinary risks of handling.

**D. Hospitals and similar institutions.**

Under this heading, but for the purpose of storage only, is included any hospital, infirmary, dispensary, clinic, nursing-home, or other institution at which human ailments are treated.

*(i) Poisons not issued for use within the institution.*

- (a) If there is a dispensing department, poisons not issued for use within the institution must be stored in that department, but subject to any rules in the institution, the pharmacist may decide upon detail;
- (b) If there is no dispensing department, poisons not issued for use within the institution must be stored in charge of a person appointed for the purpose by the governing body or person in control of the institution, and if a First Schedule poison either in a cupboard, or drawer, or on a shelf reserved solely for the storage of poisons.  
If a poison is stored on a shelf the container must be distinguishable by touch from the containers of articles other than poisons stored on the same premises.

*(ii) Poisons issued to the wards.*

Every First Schedule poison must be stored in a cupboard reserved solely for the storage of poisons and poisonous substances.

All places in which poisons are stored in hospitals and similar institutions must be inspected regularly, at intervals not exceeding three months, by a pharmacist or some other person appointed for the purpose by the governing body or person in control of the institution.

**TRANSPORT**

All poisons consigned for transport must be sufficiently strongly packed to avoid leakage arising from the ordinary risks of handling and transport. In addition, poisons which are not medicines and are included in the Eighth Schedule, and which are consigned for transport by carrier, must be labelled conspicuously on the outside of the package with the name or description of the poison as set out in the Eighth Schedule, and a notice indicating that it is to be kept separate from food and from empty foodstuff containers.

It should also be noted that any poison in the First Schedule which is lawfully sold or supplied to any person on a written order must, if sent by post, be sent by registered post.

## MANUFACTURE

In all establishments in which pharmaceutical preparations containing poison are manufactured for the internal treatment of human ailments, the preparation must be manufactured by or under the supervision of a pharmacist, a Fellow or Associate of the Institute of Chemistry, or a person who for a period of at least three years before May 1, 1936, was continuously engaged in such manufacture, and has furnished to the Registrar of the Pharmaceutical Society of Great Britain a statement in writing, verified by a statutory declaration, to that effect; except that preparations containing pituitary, suprarenal or thyroid glands, their active principles or salts of their active principles, may be manufactured by or under the supervision of a doctor.

## THE POISONS LIST.

*As amended by the Poisons List (Amendment) Orders, 1937, 1938 and 1940.*

## PART I (marked [P1] in our text).

- |   |   |
|---|---|
| Acetanilide; alkyl acetanilides                                     | Thebaine  |
| Alkali fluorides other than those specified in Part II of this List | Veratrum, alkaloids of  |
| Alkaloids, the following; their salts, simple or complex:—          | Yohimba, alkaloids of   |
| Acetyldihydrocodeinone; its esters                                  | Allylisopropylacetylurea  |
| Aconite, alkaloids of   | Amidopyrine; its salts  |
| Apomorphine   | Amino-alcohols, esterified with benzoic acid, phenylacetic acid, phenylpropionic acid, cinnamic acid or the derivatives of these acids  |
| Atropine  | Amyl nitrite  |
| Belladonna, alkaloids of  | Antimony, chlorides of; oxides of antimony; sulphides of antimony; antimonates; antimonites; organic compounds of antimony  |
| Benzoylmorphine   | Arsenical substances, the following, except those specified in Part II of this List:—arsenic, halides of; oxides of arsenic; arsenates; arsenites; organic compounds of arsenic |
| Benzylmorphine  | Barbituric acid; its salts; derivatives of barbituric acid; their salts; compounds of barbituric acid, its salts, its derivatives, their salts, with any other substance        |
| Brucine   | Barium, salts of, other than barium sulphate and the salts of barium specified in Part II of this List  |
| Calabar bean, alkaloids of  | Beta-aminopropylbenzene; its salts; its N-alkyl derivatives; their salts; beta-aminoisopropylbenzene; its salts; its N-alkyl derivatives; their salts                           |
| Coca, alkaloids of  | Butyl chloral hydrate   |
| Cocaine   | Cannabis (the dried flowering or fruiting tops of <i>Cannabis sativa</i> Linn.); the resin of cannabis; extracts of cannabis; tinctures of cannabis; cannabin tannate           |
| Codeine   | Cantharidin; cantharidates  |
| Colchicine  | Chloral formamide   |
| Coniine   | Chloral hydrate   |
| Cotarnine   | Chloroform  |
| Curarine  | Creosote obtained from wood   |
| Diacetylmorphine  | Croton, oil of  |
| Dihydrocodeinone; its esters  | Digitalis, glycosides of; other active principles of digitalis  |
| Dihydrohydroxycodone; its esters                                    |   |
| Dihydromorphine; its esters   |   |
| Dihydromorphinone; its esters                                       |   |
| Ecdonine; its esters  |   |
| Emetine   |   |
| Ephedra, alkaloids of   |   |
| Ergot, alkaloids of   |   |
| Ethylmorphine   |   |
| Gelsemium, alkaloids of   |   |
| Homatropine   |   |
| Hyosine   |   |
| Hyoscyamine   |   |
| Jaborandi, alkaloids of   |   |
| Lobelia, alkaloids of   |   |
| Morphine  |   |
| Papaverine  |   |
| Pomegranate, alkaloids of   |   |
| Quebracho, alkaloids of, other than the alkaloids of red quebracho  |   |
| Sabadilla, alkaloids of   |   |
| Solanaceous alkaloids not otherwise included in this List           |   |
| Stavesacre, alkaloids of  |   |
| Strychnine  |   |



Dinitrocresols; dinitronaphthols; dinitrophenols; dinitrothymols  
 Elaterin  
 Ergot (the sclerotia of any species of *Claviceps*); extracts of ergot; tinctures of ergot  
 Erythrityl tetranitrate  
 Glyceryl trinitrate  
 Guanidines, the following:—poly-methylene diguanidines, dipara-anisylphenetyl guanidine  
 Hydrocyanic acid; cyanides; double cyanides of mercury and zinc  
 Insulin  
 Lead acetates; compounds of lead with acids from fixed oils  
 Mannityl hexanitrate  
 Mercury, oxides of; nitrates of mercury; mercuric ammonium chlorides; potassium-mercuric iodides; mercuric oxycyanides; mercuric thiocyanate  
 Metanitrophenol; orthonitrophenol; paranitrophenol  
 Nux Vomica  
 Opium  
 Orthocaine; its salts  
 Ouabain  
 Oxalic acid  
 Oxycinchonic acid, derivatives of; their salts; their esters  
 Para-aminobenzenesulphonamide; its salts; derivatives of para-aminobenzenesulphonamide having any of the hydrogen atoms of the para-amino group or of the sulphonamide

group substituted by another radical; their salts  
 Para-amino-benzoic acid; esters of; their salts  
 Phenetidylphenacetin  
 Phenols (any member of the series of phenols of which the first member is phenol and of which the molecular composition varies from member to member by one atom of carbon and two atoms of hydrogen) except in substances containing less than sixty per cent., weight in weight, of phenols; compounds of phenol with a metal, except in substances containing less than the equivalent of sixty per cent., weight in weight, of phenols  
 Phenylcinchoninic acid; salicylcinchonic acid; their salts; their esters  
 Phenylethylhydantoin; its salts; its acyl derivatives; their salts  
 Phosphorus, yellow  
 Picric acid  
 Picrotoxin  
 Pituitary gland, the active principles of  
 Savin, oil of  
 Strophanthus; glycosides of strophanthus  
 Sulphonal; alkyl sulphonals  
 Suprarenal gland, the active principles of; their salts  
 Thallium, salts of  
 Thyroid gland, the active principles of; their salts  
 Tribromethyl alcohol

## PART II (marked [P2] in our text).

Ammonia  
 Arsenical substances, the following:—  
 Arsenic sulphides  
 Arsenious oxide  
 Calcium arsenates  
 Calcium arsenites  
 Copper acetoarsenites  
 Copper arsenates  
 Copper arsenites  
 Lead arsenates  
 Potassium arsenites  
 Sodium arsenates  
 Sodium arsenites  
 Sodium thioarsenates  
 Barium, salts of, the following:—  
 Barium carbonate  
 Barium silicofluoride  
 Formaldehyde  
 Hydrochloric acid  
 Hydrofluoric acid; potassium fluoride; sodium fluoride; sodium silicofluoride

Mercuric chloride; mercuric iodide; organic compounds of mercury  
 Metallic oxalates  
 Nicotine; its salts  
 Nitric acid  
 Nitrobenzene  
 Phenols as defined in Part I of this List in substances containing less than sixty per cent., weight in weight, of phenols; compounds of phenol with a metal in substances containing less than the equivalent of sixty per cent., weight in weight, of phenols  
 Phenylene diamines; toluene diamines; other alkylated-benzene diamines; their salts  
 Potassium hydroxide  
 Sodium hydroxide  
 Sulphuric acid

(Note.—Several poisons in this List are exempted by the Poisons Rules (Rule 11 and Third Schedule, pages 1122 to 1124), made by the Secretary of State under the Pharmacy and Poisons Act, 1933, from the application of the Act when present in certain specified substances or articles.)

**SCHEDULES TO THE POISONS RULES, 1935.**

*As amended by the Poisons (Amendment) Rules, 1937, 1938 and 1940.*

**FIRST SCHEDULE (marked [S1] in our text).**

*Substances falling within the Poisons List, see pages 1118 to 1119, to which special restrictions apply.*

Alkaloids, the following; their salts, simple or complex:—

- Acetyldihydrocodeinone
- Aconite, alkaloids of, except substances containing less than 0·02 per cent. of the alkaloids of aconite
- Apomorphine except substances containing less than 0·2 per cent. of apomorphine
- Atropine except substances containing less than 0·15 per cent. of atropine
- Belladonna, alkaloids of, except substances containing less than 0·15 per cent. of the alkaloids of belladonna calculated as hyoscyamine
- Benzoylmorphine
- Benzylmorphine
- Brucine except substances containing less than 0·2 per cent. of brucine
- Calabar bean, alkaloids of
- Coca, alkaloids of, except substances containing less than 0·1 per cent. of the alkaloids of coca
- Cocaine except substances containing less than 0·1 per cent. of cocaine
- Codeine except substances containing less than one per cent. of codeine
- Colchicine except substances containing less than 0·5 per cent. of colchicine
- Coniine except substances containing less than 0·1 per cent. of coniine
- Cotarnine except substances containing less than 0·2 per cent. of cotarnine
- Curarine
- Diacylmorphine
- Dihydrocodeinone
- Dihydrohydroxycodeinone
- Dihydromorphine
- Dihydromorphine
- Ecgonine except substances containing less than 0·1 per cent. of ecgonine
- Emetine except substances containing less than one per cent. of emetine
- Ergot, alkaloids of
- Ethylmorphine except substances containing less than 0·2 per cent. of ethylmorphine
- Gelsemium, alkaloids of, except substances containing less than 0·1 per cent. of the alkaloids of gelsemium
- Homatropine except substances containing less than 0·15 per cent. of homatropine
- Hyoscine except substances containing less than 0·15 per cent. of hyoscine
- Hyoscyamine except substances containing less than 0·15 per cent. of hyoscyamine
- Jaborandi, alkaloids of, except substances containing less than 0·5 per cent. of the alkaloids of jaborandi
- Lobelia, alkaloids of, except substances containing less than 0·5 per cent. of the alkaloids of lobelia.
- Morphine except substances containing less than 0·2 per cent. of morphine calculated as anhydrous morphine
- Nicotine
- Papaverine except substances containing less than one per cent. of papaverine
- Pomegranate, alkaloids of, except substances containing less than 0·5 per cent. of the alkaloids of pomegranate
- Quebracho, alkaloids of
- Sabadilla, alkaloids of, except substances containing less than one per cent. of the alkaloids of sabadilla
- Solanaceous alkaloids, not otherwise included in this Schedule, except substances containing less than 0·15 per cent. of solanaceous alkaloids calculated as hyoscyamine
- Stavesacre, alkaloids of, except substances containing less than 0·2 per cent. of the alkaloids of stavesacre

- Strychnine except substances containing less than 0.2 per cent. of strychnine  
 Thebaine except substances containing less than one per cent. of thebaine  
 Veratrum, alkaloids of, except substances containing less than one per cent. of the alkaloids of veratrum  
 Yohimbin, alkaloids of
- Allylisopropylacetylurea  
 Amidopyrine; its salts  
 Amino-alcohols, esterified with benzoic acid, phenylacetic acid, phenylpropionic acid, cinnamic acid or the derivatives of these acids, except in substances containing less than ten per cent. of esterified amino-alcohols  
 Antimonial poisons except substances containing less than the equivalent of one per cent. of antimony trioxide  
 Arsenical poisons except substances containing less than the equivalent of 0.01 per cent. of arsenic trioxide and except dentifrices containing less than 0.5 per cent. of acetarsol  
 Barbituric acid; its salts; derivatives of barbituric acid; their salts; compounds of barbituric acid, its salts, its derivatives, their salts, with any other substance  
 Barium, salts of  
 Beta-aminopropylbenzene; its salts; its N-alkyl derivatives; their salts; beta-aminoisopropylbenzene; its salts; its N-alkyl derivatives; their salts  
 Cannabis; the resin of cannabis; extracts of cannabis; tinctures of cannabis; cannabin tannate  
 Cantharidin except substances containing less than 0.01 per cent. of cantharidin  
 Cantharidates except substances containing less than the equivalent of 0.01 per cent. of cantharidin  
 Digitalis, glycosides and other active principles of, except substances containing less than one unit of activity (as defined in the British Pharmacopœia) in two grammes of the substance  
 Dinitrocresols; dinitronaphthols; dinitrophenols; dinitrothymols  
 Ergot; extracts of ergot; tinctures of ergot  
 Guanidines, the following:—polymethylene diguanidines, dipara-anisylphenetyl guanidine  
 Hydrocyanic acid except substances containing less than 0.15 per cent., weight in weight, of hydrocyanic acid (HCN); cyanides except substances containing less than the equivalent of 0.1 per cent., weight in weight, of hydrocyanic acid (HCN); double cyanides of mercury and zinc  
 Lead, compounds of, with acids from fixed oils  
 Mercuric chloride except substances containing less than one per cent. of mercuric chloride; mercuric iodide except substances containing less than two per cent. of mercuric iodide; nitrates of mercury except substances containing less than the equivalent of three per cent., weight in weight, of mercury (Hg); potassio-mercuric iodides except substances containing less than the equivalent of one per cent. of mercuric iodide; organic compounds of mercury except substances containing less than the equivalent of 0.2 per cent., weight in weight, of mercury (Hg)  
 Metanitrophenol; orthonitrophenol; paranitrophenol  
 Nux Vomica except substances containing less than 0.2 per cent. of strychnine  
 Opium except substances containing less than 0.2 per cent. of morphine calculated as anhydrous morphine  
 Ouabain  
 Oxycinchonic acid, derivatives of; their salts; their esters  
 Para-aminobenzenesulphonamide; its salts; derivatives of para-aminobenzenesulphonamide having any of the hydrogen atoms of the para-amino group or of the sulphonamide group substituted by another radical; their salts  
 Phenetidylphenacetin  
 Phenylcinchoninic acid; salicyl-cinchonic acid; their salts; their esters  
 Phenylethylhydantoin; its salts; its acyl derivatives; their salts  
 Picrotoxin  
 Savin, oil of  
 Strophanthus, glycosides of  
 Sulphonals; alkyl sulphonals  
 Thallium, salts of  
 Tribromethyl alcohol

## SECOND SCHEDULE.

*Poisons exempted by Rule 5 (2) from labelling provisions when sold or supplied in certain circumstances.*

Alkali fluorides  
 Ammonia  
 Antimony, chlorides of; oxides of antimony; sulphides of antimony; antimonates; antimonites  
 Chloroform  
 Dinitrocresols; dinitronaphthols; dinitrophenols  
 Formaldehyde  
 Glyceryl trinitrate  
 Hydrochloric acid  
 Hydrofluoric acid; sodium silicofluoride  
 Lead acetates; compounds of lead with acids from fixed oils  
 Mercuric chloride; mercuric iodide; organic compounds of mercury  
 Mercury, oxides of; nitrates of mercury  
 Metanitrophenol; orthonitrophenol; paranitrophenol  
 Nitric acid  
 Nitrobenzene  
 Oxalic acid; metallic oxalates  
 Phenols; compounds of phenol with a metal  
 Phosphorus, yellow  
 Picric acid  
 Potassium hydroxide  
 Sodium hydroxide  
 Sulphuric acid

## THIRD SCHEDULE (marked [§3] in our text).

*Articles exempted by Rule 11 from the provisions of the Act and of these Rules.*

## GROUP I.

## GENERAL EXEMPTIONS.

Adhesives; anti-fouling compositions; builders' materials; ceramics; distempers; electrical valves; enamels; explosives; fillers; fireworks; glazes; glue; inks; lacquer solvents; loading materials; matches; motor fuels and lubricants; paints other than pharmaceutical paints; photographic paper; pigments; plastics; propellants; rubber; varnishes.

## GROUP II.

## SPECIAL EXEMPTIONS.

<i>Poison.</i>	<i>Substance or article in which exempted.</i>
Acetanilide; alkyl acetanilides	Substances not being preparations for the treatment of human ailments
Alkaloids	
Emetine	Ipecacuanha; extracts and tinctures of ipecacuanha; substances containing less than 0.05 per cent. of emetine
Ephedra, alkaloids of	Substances containing less than one per cent. of the alkaloids of ephedra
Jaborandi, alkaloids of	Substances containing less than 0.025 per cent. of the alkaloids of jaborandi
Lobelia, alkaloids of	Preparations for the relief of asthma in the form of cigarettes, smoking mixtures or fumigants; substances containing less than 0.1 per cent. of the alkaloids of lobelia
Nicotine	Tobacco
Pomegranate, alkaloids of	Pomegranate bark
Solanaceous alkaloids	Stramonium contained in preparations for the relief of asthma in the form of cigarettes, smoking mixtures or fumigants
Stavesacre, alkaloids of	Soaps; ointments; lotions for external use

**Ammonia**

Substances not being solutions of ammonia or preparations containing solutions of ammonia; substances containing less than five per cent., weight in weight, of ammonia ( $\text{NH}_3$ ); refrigerators; smelling bottles

**Antimony, chlorides of**

Polishes

**Arsenical poisons**

Pyrites ores or sulphuric acid containing arsenical poisons as natural impurities

**Barium, salts of**

Witherite other than finely ground witherite

**Beta-aminopropylbenzene; its salts; its N-alkyl derivatives; their salts; beta-aminoisopropylbenzene; its salts; its N-alkyl derivatives; their salts**

Appliances for inhalation in which the poison is absorbed in inert solid material

**Chloroform**

Substances containing less than ten per cent. of chloroform

**Cresote obtained from wood**

Substances containing less than fifty per cent. of cresote obtained from wood

**Dinitrocresols**

Substances not being preparations for the treatment of human ailments

**Dinitrophenols**

Substances not being preparations for the treatment of human ailments

**Formaldehyde**

Substances containing less than five per cent., weight in weight, of formaldehyde ( $\text{H}\cdot\text{CHO}$ ); photographic glazing or hardening solutions

**Hydrochloric acid**

Substances containing less than nine per cent., weight in weight, of hydrochloric acid ( $\text{HCl}$ )

**Lead acetate**

Substances containing less than four per cent. of lead acetate

**Lead, compounds of**

Machine-spread plasters

**Mercuric chloride**

Batteries

**Mercuric chloride; mercuric iodide; organic compounds of mercury**

Dressings on seeds or bulbs

**Mercury, nitrates of**

Ointments containing less than the equivalent of three per cent., weight in weight, of mercury ( $\text{Hg}$ )

**Nitric acid**

Substances containing less than nine per cent., weight in weight, of nitric acid ( $\text{HNO}_3$ )

**Nitrobenzene**

Substances containing less than 0.1 per cent. of nitrobenzene; soaps containing less than one per cent. of nitrobenzene; polishes

**Oxalic acid; metallic oxalates**

Laundry blue; polishes

**Phenols**

Carvacrol; creosote obtained from coal tar; essential oils in which phenols occur naturally; medicines containing less than one per cent. of phenols;

nasal sprays, mouth-washes, pastilles, lozenges, capsules, pessaries, ointments, or suppositories containing less than 2.5 per cent. of phenols;

smelling bottles;

soaps for washing;

solid substances, other than pastilles, lozenges, capsules, pessaries, ointments and suppositories, containing less than sixty per cent. of phenols;

tar (coal or wood), crude or refined;

tertiary butyl-cresol;

thymol

Substances other than preparations for the dyeing of hair

**Phenylene diamines; toluene diamines; other alkylated-benzene diamines; their salts**

NN\*

Picric acid	Substances containing less than five per cent. of picric acid
Potassium hydroxide	Substances containing less than twelve per cent. of potassium hydroxide; accumulators; batteries
Sodium ethylmercurithio-salicylate	Therapeutic substances containing less than 0.1 per cent. of sodium ethylmercurithio-salicylate as a preservative
Sodium fluoride	Substances containing less than three per cent. of sodium fluoride as a preservative
Sodium hydroxide	Substances containing less than twelve per cent. of sodium hydroxide
Sodium silicofluoride	Substances containing less than three per cent. of sodium silicofluoride as a preservative
Sulphuric acid	Substances containing less than nine per cent., weight in weight, of sulphuric acid ( $H_2SO_4$ ); accumulators; batteries; fire extinguishers.

## FOURTH SCHEDULE (marked [84] in our text).

*Substances required by Rule 12 to be sold by retail only upon a prescription given by a qualified medical practitioner, registered dentist or registered veterinary surgeon.*

Amidopyrine; its salts  
 Barbituric acid; its salts; derivatives of barbituric acid; their salts; compounds of barbituric acid, its salts, its derivatives, their salts; with any other substance  
 Dinitroresols; dinitronaphthols; dinitrophenols; dinitrothymols  
 Para-aminobenzenesulphonamide; its salts; derivatives of para-aminobenzenesulphonamide having any of the hydrogen atoms of the para-amino group or of the sulphonamide group substituted by another radical; their salts  
 Phenylcinchoninic acid; salicyl-cinchoninic acid; their salts; their esters  
 Sulphonals; alkyl sulphonals

## FIFTH SCHEDULE.

*Form to which the substances specified are restricted when sold by listed sellers of Part II poisons (Rule 14 (2) (a)).*

<i>Poison.</i>	<i>Form to which sale is restricted.</i>
Arsenical substances—	
Arsenious oxide	Sheep dips, sheep washes
Arsenic sulphides	"
Calcium arsenates	Agricultural and horticultural insecticides or fungicides
Calcium arsenites	" " " "
Copper acetoarsenite	" " " "
Copper arsenates	" " " "
Copper arsenites	" " " "
Lead arsenates	" " " "
Potassium arsenites	" " " "
Sodium arsenates	Sheep dips, sheep washes
Sodium arsenites	" " " "
Sodium thioarsenates	" " " "
Barium carbonate	Preparations for the destruction of rats and mice

## Mercurial substances—

Mercuric chloride

Mercuric iodide

Organic compounds of  
mercuryMetallic oxalates other than  
potassium quadroxalate

Nitrobenzene

Agricultural and horticultural fungicides,  
seed and bulb dressings, insecticides  
Agricultural and horticultural fungicides,  
seed and bulb dressings

" " "

Photographic solutions or materials

Agricultural and horticultural insecticides;  
substances for the treatment of bee disease;  
ointments for the treatment of animals

## SIXTH SCHEDULE (marked [86] in our text).

*Statement of particulars as to proportion of the poison in certain cases permitted  
by Rule 18 (2).**Name of Poison.**Particulars.*

## Alkaloids

Aconite, alkaloids of

The proportion of any one alkaloid of aconite  
that the preparation would be calculated to  
contain on the assumption that all the  
alkaloids of aconite in the preparation were  
that alkaloid.The same as above, with the substitution for  
the reference to aconite of a reference to  
belladonna, calabar bean or such other of  
the said poisons as the case may require.

Belladonna, alkaloids of

Calabar bean, alkaloids of

Coca, alkaloids of

Ephedra, alkaloids of

Ergot, alkaloids of

Gelsemium, alkaloids of

Jaborandi, alkaloids of

Lobelia, alkaloids of

Pomegranate, alkaloids of

Quebracho, alkaloids of,

other than the alkaloids

of red quebracho

Sabadilla, alkaloids of

Solanaceous alkaloids not

otherwise included in

the Poisons List

Stavesacre, alkaloids of

Veratrum, alkaloids of

Yohimba, alkaloids of

## Antimonial poisons

The proportion of antimony trioxide ( $\text{Sb}_2\text{O}_3$ )  
or antimony pentoxide ( $\text{Sb}_2\text{O}_5$ ) that the  
preparation would be calculated to contain  
on the assumption that the antimony (Sb)  
in the poison had been wholly converted  
into antimony trioxide or antimony pent-  
oxide as the case may be.

## Arsenical poisons

The proportion of arsenic trioxide ( $\text{As}_2\text{O}_3$ ) or  
arsenic pentoxide ( $\text{As}_2\text{O}_5$ ) that the prepara-  
tion would be calculated to contain on the  
assumption that the arsenic (As) in the  
poison had been wholly converted into  
arsenic trioxide or arsenic pentoxide as the  
case may be.

## Barium, salts of

The proportion of one particular barium salt  
which the preparation would be calculated  
to contain on the assumption that the  
barium (Ba) in the poison had been wholly  
converted into that salt.

Digitalis, glycosides of; other active principles of digitalis	The number of units of activity as defined in the British Pharmacopœia contained in a specified quantity of the preparation.
Hydrocyanic acid; cyanides; double cyanides of mercury and zinc	The proportion of hydrocyanic acid (HCN) that the preparation would be calculated to contain on the assumption that the cyanides in the poison had been wholly converted into hydrocyanic acid.
Insulin	The number of units of activity as defined in the British Pharmacopœia contained in a specified quantity of the preparation.
Lead, compounds of, with acids from fixed oils	The proportion of lead oxide (PbO) that the preparation would be calculated to contain on the assumption that the lead in the poison had been wholly converted into lead oxide.
Mercury, organic compounds of	The proportion of organically-combined mercury (Hg) contained in the preparation.
Nux Vomica	The proportion of strychnine contained in the preparation.
Opium	The proportion of morphine contained in the preparation.
Phenols	The proportion of phenols (added together) contained in the preparation.
Compounds of phenol with a metal	The proportion of phenols (added together) that the preparation would be calculated to contain on the assumption that the compounds of phenols with a metal had been wholly converted into the corresponding phenols.
Pituitary gland, the active principles of	Either— <ol style="list-style-type: none"> <li>(a) the number of units of activity as defined in the British Pharmacopœia contained in a specified quantity of the preparation; or</li> <li>(b) the proportion of pituitary gland, or of anterior or of posterior lobe of the gland, as the case may be, contained in the preparation; or</li> <li>(c) the amount of pituitary gland, or of anterior or of posterior lobe of the gland, as the case may be, from which a specified quantity of the preparation was obtained, together with an indication whether the amount relates to fresh or to dried gland substance.</li> </ol>
Potassium hydroxide	The proportion of potassium monoxide ( $K_2O$ ) which the preparation would be calculated to contain on the assumption that the potassium hydroxide in the preparation had been wholly converted into potassium monoxide.
Sodium hydroxide	The proportion of sodium monoxide ( $Na_2O$ ) which the preparation would be calculated to contain on the assumption that the sodium hydroxide in the preparation had been wholly converted into sodium monoxide.
Strophanthus, glycosides of	The amount of Standard Tincture of Strophanthus as defined in the British Pharmacopœia which possesses the same activity as a specified quantity of the preparation when assayed by the method described in the said Pharmacopœia.



Suprarenal gland, the active principles of; their salts

Either—

- (a) the proportion of suprarenal gland or of the cortex or of the medulla of the gland, as the case may be, contained in the preparation; or
- (b) the amount of suprarenal gland, or of the cortex or of the medulla of the gland, as the case may be, from which a specified quantity of the preparation was obtained, together with an indication whether the amount relates to fresh or to dried gland substance.

Thyroid gland, the active principles of; their salts

Either—

- (a) the proportion of thyroid gland contained in the preparation; or
- (b) the amount of thyroid gland from which a specified quantity of the preparation was obtained, together with an indication whether the amount relates to fresh or to dried gland.

SEVENTH SCHEDULE (marked [87] in our text, except substances to which clause 2 of this schedule applies).

*Indication of character prescribed by Rule 19 for the purposes of section 18 (1) (c) (iii) of the Act.*

1. To be labelled with the words "*Caution. It is dangerous to take this preparation except under medical supervision.*":—

Medicines made up ready for the internal treatment of human ailments if the poison is one of the following:—

Allylisopropylacetylurea

Beta-aminopropylbenzene; its salts; its N-alkyl derivatives; their salts; beta-aminoisopropylbenzene; its salts; its N-alkyl derivatives; their salts

Insulin

Phenylethylhydantoin; its salts; its acyl derivatives; their salts

Pituitary gland, the active principles of

Thyroid gland, the active principles of; their salts

2. To be labelled with the words "*Caution. It is dangerous to exceed the stated dose.*":—

Medicines (other than medicines mentioned in paragraph 1 of this Schedule) made up ready for the internal treatment of human ailments except in the case of a substance included in the First Schedule.

3. To be labelled with the words "*Poison. For animal treatment only.*":—

Medicines made up ready for the treatment of animals.

4. To be labelled with the words "*Caution. This preparation may cause serious inflammation of the skin in certain persons and should be used only in accordance with expert advice.*":—

Preparations for the dyeing of hair containing phenylene diamines, toluene diamines or other alkylated-benzene diamines or their salts.

5. To be labelled with the words "*Caution. This substance is caustic.*":—

Potassium hydroxide, sodium hydroxide, and articles containing either of those substances.

#### EIGHTH SCHEDULE.

*Poisons to which Rule 25 (Transport) applies.*

Arsenical poisons; barium, salts of; hydrocyanic acid; cyanides; nicotine; strychnine; thallium, salts of

#### NINTH SCHEDULE.

*Form of application to be made to the local authority by a person desiring his name to be entered in the list kept by local authorities in pursuance of section 21 of the Act. (Rule 30 (1).)*

## TENTH SCHEDULE.

*Form of the list to be kept by local authorities in pursuance of section 21 (1) of the Act. (Rule 30 (3).)*

## ELEVENTH SCHEDULE.

*Certificate for the purchase of a poison. (Rule 31.)*

## TWELFTH SCHEDULE.

*Form of entry required by Rule 32 to be made in the book to be kept by sellers of poisons in accordance with section 18 (2) (b) of the Act.*

*(For further details of Schedules 9 to 12 see Vol. I, 21st Edn.)*

## THIRTEENTH SCHEDULE.

*(Inserted in accordance with the Poisons (Amendment) (No. 2) Rules, 1940.*

*Authority for the purchase of strychnine in pursuance of proviso (e) to Rule 15.*

I hereby authorise (a).....to purchase within three months of the date hereof, (b)..... ounces of strychnine for the purpose of killing moles.

.....

Signature of      Chairman  
                     Executive Officer } \* of the.....  
                     Secretary

County War Agricultural Executive Committee. } \*  
Agricultural Executive Committee.

Date.....

(a) Insert full name of intending purchaser.

(b) Insert amount authorised to be purchased which must not exceed four ounces.

\* Delete words which do not apply

**PHARMACY AND POISONS ACT (NORTHERN IRELAND), 1925.**  
**Schedule of Poisons Applicable to Northern Ireland**  
*(as amended to 1940)*

**PART I.**

**Aconite, Aconitine** and their preparations.

**Alkaloids.** All poisonous alkaloids not specifically named in this Schedule, and their salts, and all poisonous derivatives of alkaloids.

**Arsenic** and its preparations.

**Atropine** and its salts and their preparations.

**Belladonna** and all preparations or admixtures (except belladonna plasters) containing 0.1 or more per cent. of belladonna alkaloids.

**Cannabis**, the dried flowering or fruiting tops of the pistillate plant of *C. sativa*, and the resins prepared therefrom.

**Cantharides** and its poisonous derivatives.

**Chloral Hydrate** and all its preparations.

**Coca**, any preparation or admixture of, containing 0.1 or more per cent. of coca alkaloids.

**Corrosive Sublimate** and preparations of corrosive sublimate.

**Cyanide of Potassium** and all poisonous cyanides and their preparations.

**Diamorphine** (also known as **Heroin**) and all preparations or admixtures containing 0.1 per cent. of diamorphine.

**Diethyl-Barbituric Acid** and other alkyl, aryl or metallic derivatives of barbituric acid, whether described as Veronal, Proponal, Medinal, or by any other trade name, mark or designation, and all poisonous urethanes and ureides.

**Digitalin** and all other poisonous constituents of digitalis.

**Dinitro Phenols, Dinitro Cresols**, preparations or admixtures containing dinitro phenols, preparations or admixtures containing dinitro cresols.

**Ecgonine** and all preparations and admixtures containing 0.1 per cent. of ecgonine.

**Emetic Tartar** and all preparations or admixtures containing 1 or more per cent. of emetic tartar.

**Ergot of Rye** and preparations of ergots.

**Lead**, in combination with oleic acid, or other higher fatty acids, whether sold as Diachylon or under any other designation (except machine-spread plasters).

**Nux Vomica** and all preparations or admixtures containing 0.2 or more per cent. of strychnine.

**Opium** and all preparations or admixtures containing 0.2 or more per cent. of morphine.

**Phenylcinchoninic Acid**, its salts, its esters; derivatives of phenylcinchoninic acid, their salts, their esters; preparations and admixtures containing phenylcinchoninic acid, its salts, its esters; preparations and admixtures containing derivatives of phenylcinchoninic acid, their salts, their esters.

**Picrotoxin**.

**Prussic Acid** and all preparations or admixtures containing 0.1 or more per cent. of prussic acid.

**Savin** and its oil, and all preparations or admixtures containing savin or its oil.

**Strophanthin** and all other poisonous constituents of strophanthus.

**Strychnine**, all preparations and admixtures containing 0.2 or more per cent. of strychnine.

**Sulphuric Ether**.

**Tobacco**, any preparations or admixtures of (except tobacco prepared for smoking and snuff), containing the poisonous alkaloids of tobacco.

## PART II.

**Almonds, Essential Oil of** (unless deprived of prussic acid).

**Antimonial Wine**.

**Barium, Salts of**, except barium sulphate.

**Cantharides**, tincture and all vesicating liquid preparations or admixtures of.

**Carbolic Acid**, and liquid preparations of carbolic acid, and its homologues containing more than 3 per cent. of those substances.

**Chloroform** and all preparations or admixtures containing more than 20 per cent. of chloroform.

**Digitalis**.

**Mercury, Ammoniated (White Precipitate)**.

**Mercury, Biniiodide (Mercuric Iodide)**.

**Mercury, Red Oxide (Red Precipitate)** and all oxides of.

**Mercuric Sulphocyanide**.

**Oxalic Acid**.

**Phosphorus** and all preparations and admixtures containing it in a free state (except lucifer matches).

**Poppies**, all preparations of, except red poppy petals and syrup of red poppies (*Papaver rhæas*).

**Strophanthus**.

**Sulphonal** and its homologues, whether described as Trional, Tetronal or by any other trade mark, name or designation.

**Zinc Chloride** and liquid preparations of zinc chloride, except preparations intended to be used for soldering, or other purely industrial purpose, provided that they are contained in closed vessels labelled with the word "Poisonous,"

and bearing the name and address of the seller and a notice of the special purpose for which the preparations are intended.

All preparations or admixtures which are not included in Part I of this Schedule, and contain a poison within the meaning of this Act, except tobacco prepared for smoking and snuff, machine-spread lead plasters, preparations or admixtures the exclusion of which from this Schedule is indicated by the words therein relating to chloroform, and except such substances as come within the provisions of Section 5 of the Poisons and Pharmacy Act, 1908.

**SALE OF POISONS (IRELAND) ACT, 1870.**  
**Schedule of Poisons Applicable to Eire**  
*(as amended to 1940)*

**PART I.**

**Aconite** and its preparations.  
**Alkaloids**, *see* Strychnine.  
**Arsenic** and its preparations.  
**Barbituric Acid**; its salts; derivatives of barbituric acid; their salts; compounds of barbituric acid; its salts; its derivatives; their salts; with any other substance.  
**Cantharides**.  
**Coca**, any preparation or admixture of, containing 1 or more per cent. of coca alkaloids.  
**Corrosive Sublimate**.  
**Cyanide of Potassium** and all metallic cyanides.  
**Diamorphine** (also known as heroin) and all preparations or admixtures containing 0.1 per cent. of diamorphine.  
**Ecgonine** and all preparations or admixtures containing 0.1 per cent. of ecgonine.  
**Emetic Tartar**.  
**Ergot of Rye** and its preparations.  
**Opium** and all preparations or admixtures containing 0.2 or more per cent. of morphine.  
**Prussic Acid**.  
**Savin** and its oil.  
**Strychnine** and all poisonous vegetable alkaloids and their salts.

**PART II.**

**Almonds, Essential Oil of**, unless deprived of its prussic acid.  
**Ammoniated Mercury**.  
**Belladonna** and its preparations.  
**Benzedrine** and its salts.  
**Cantharides**, the tincture and all vesicating liquid preparations of.  
**Carbolic Acid**, *see* Phenol.  
**Chloral Hydrate** and all its preparations.  
**Chloroform**.  
**Corrosive Sublimate**, preparations of.  
**Diethyl Barbituric Acid** and other alkyl, aryl, or metallic derivatives of barbituric acid, whether described as Veronal, Proponal, Medinal or by any other trade name, mark or designation; and all poisonous urethanes and ureides.  
**Ether, Sulphuric**.  
**Mercury, Biniode of**.  
**Mercury, Red Oxide of**.  
**Morphine**, preparations of.  
**Nux Vomica** and its preparations.  
**Opium** and all preparations of opium or poppies.  
**Oxalic Acid** and all oxalates.  
**Phenol**, commonly called carbolic acid, and its homologues containing not more than nine carbon atoms, and all preparations and admixtures thereof, except tooth-pastes, tooth-powders and soaps for washing.  
**Phosphorus** and all preparations containing it in a free state.  
**Poppies**, all preparations of, *see* Opium.  
**Strychnine**, preparations of.  
**Synthetic Ephedrine Alkaloids** and their salts.  
**Thallium**, salts of.  
**Every Compound** containing any of the poisons mentioned in this Schedule when prepared or sold for the destruction of vermin.

**SUMMARY OF DANGEROUS DRUGS LEGISLATION****Main Points to Remember in Prescribing and Dispensing**

The drugs (marked [D] in our text) to which the Acts apply are set out on pages 1133 and 1134.

For exempted preparations see pages 1139 and 1140.

*Specimen form of prescription for "dangerous drugs."***1. Doctor.**

[Address of  
prescriber.]\*

[Name and address of  
patient.]

[Name and quantity of drug,  
or of B.P., B.P.C. or Drug  
Tariff preparation contain-  
ing it.]

[See footnote if the prescription is to be repeated]†

[Date (to be inserted  
by prescriber).]

[Signature (not initials)  
of prescriber.]

**2. Dentist.**

As above, but in addition the words "For local dental treatment only" must be written on the prescription.

**3. Veterinary Surgeon.**

As for doctor's prescription except that the "name and address of the person to whom the medicine is to be delivered" must be inserted in place of the "name and address of patient," and the words "For animal treatment only" must be written on the prescription.

\*Address of doctor is not necessary in the case of National Health Insurance prescriptions.

†The maximum number of times which a prescription may be ordered to be repeated is two (i.e., it may be dispensed three times in all) and the prescriber must either state the actual dates upon which the medicine may be repeated, or indicate what period of time must elapse before repeating on any occasion.

**When dispensing a prescription the pharmacist must**

- (i) know the signature of the prescriber;
- (ii) be satisfied that the prescription is genuine. He should make sure if possible that the doctor, dentist, or veterinary surgeon is authorised to prescribe "dangerous drugs";
- (iii) mark the prescription with the date on which it is dispensed;
- (iv) retain the prescription for two years, except Health prescriptions;
- (v) make the required records in the "dangerous drugs" register on the same or following day on which the prescription is dispensed;
- (vi) keep the register, which must be a bound book, in some part of the premises to which it relates so as to be *at all times* available for inspection;
- (vii) make a copy of the prescription in the prescription book, except Health prescriptions.

**Sales to doctors, dentists, and veterinary surgeons**

The requirements in regard to sales of First Schedule poisons, set out on page 1113, must be complied with and, in addition, records must be made in the "dangerous drugs" register.

### SPECIMEN FORM OF "SIGNED ORDER" OF DOCTOR, DENTIST AND VETERINARY SURGEON.

Please supply:—

[Name and quantity of drugs required.]

These drugs are required for use in my medical\* practice.]

[Signature (not initials) of practitioner.]

**Other points of assistance**

All dangerous drugs must be kept in a locked receptacle, the key being kept only by a pharmacist.

All dangerous drugs are [P1-S1] poisons.

Dentists' and veterinary surgeons' (not doctors') prescriptions must have the amount of the dangerous drugs stated on the label.

Typewritten prescriptions are accepted as written.

Doctors may write prescriptions for themselves.

Telephone orders from medical practitioners may be accepted, but the written order must follow within twenty-four hours.

Nursing homes are not authorised persons.

A foreign doctor, dentist, or veterinary surgeon is not authorised to prescribe, or be in possession of, dangerous drugs unless he is registered in Great Britain.

**DANGEROUS DRUGS ACT, 1920, SUMMARISED.**

(10 AND 11 GEO. V, CHAPTER 46.)

*With the amendments of the 1923, 1925 and 1932 Acts incorporated.*  
[D] throughout our pages means drugs or preparations coming within the provisions of these Acts.

*In this Summary "medical practitioner" means "duly qualified," i.e., registered in the Medical Register kept by the General Medical Council, 44 Hallam Street, London, W.1; "dentist" means "registered dentist"; "veterinary surgeon" means "registered veterinary surgeon."*

\*A dentist should replace the word "medical" with the word "dental," and a veterinary surgeon with the word "veterinary."

**PART I.—Raw Opium, Coca Leaves and Indian Hemp.** *Sections 1 to 3* prohibit, except under licence and at approved ports, the importation into and exportation from the United Kingdom of raw opium, coca leaves, Indian hemp, resins obtained from Indian hemp and all preparations of which such resins form the base. Where the importation of any of the above-named drugs is prohibited in any foreign country, the Secretary of State may make such conditions in regard to the licence as he deems necessary to prevent exportation from the United Kingdom to that foreign country. The Secretary of State is also empowered to make regulations controlling the production, possession, sale and distribution of these drugs. A summary of these regulations appears on pages 1143 to 1145.

**PART II.—Prepared Opium.** *Section 4.*—Import and export totally and unconditionally prohibited. *Section 5.*—Any person manufacturing, selling, dealing in, or having in possession prepared opium, or being occupier of premises used for preparation of opium for smoking, or sale or smoking of prepared opium, or being concerned in managing premises so used, or having pipes or utensils for smoking opium or preparing opium for smoking, or smoking or otherwise using prepared opium, or frequenting a place used for smoking, is guilty of offence against this Act.

**PART III.—Cocaine, Morphine, etc.** (as detailed in Section 8 below). *Section 6.*—Import and export prohibited, except under licence.

*Section 7. Sub-section 1.*—Provides for the making of regulations controlling the manufacture, sale, possession and distribution of drugs to which this part (Part III) of this Act applies. *Sub-section 2.*—The regulations so made shall provide for authorising any person lawfully carrying on a chemist's business (a) to manufacture at the shop in the ordinary course of his retail business any preparation, admixture or extract of any drug to which this Part of this Act applies; or (b) to carry on at the shop the business of retailing, dispensing or compounding any such drug. This authorisation shall be subject to the power of the Secretary of State, after consulting the Council of the Pharmaceutical Society of Great Britain, withdrawing it from any person convicted of an offence under this Act. *Sub-section 3.*—Nothing in the regulations made under this section shall derogate from the provisions of the Pharmacy Act, 1868, as amended.

*Section 8. Sub-section 1.*—The drugs to which this part of the Act applies are

- (a) medicinal opium;
- (b) any extract or tincture of Indian hemp;
- (c) morphine and its salts, and diacetylmorphine (commonly known as diamorphine or heroin) and the other esters of morphine and their respective salts;
- (d) cocaine (including synthetic cocaine) and ecgonine and their respective salts, and the esters of ecgonine and their respective salts;
- (e) any solution or dilution of morphine or cocaine or their salts in an inert substance, whether liquid or solid, containing any proportion of morphine or cocaine, and any preparation, admixture, extract or other substance (not being such a solution or dilution as aforesaid) containing not less than one-fifth per cent. of morphine or one-tenth per cent. of cocaine or of ecgonine;
- (f) any preparation, admixture, extract or other substance containing any proportion of diacetylmorphine;
- (g) dihydroxycodeinone, dihydrocodeinone, dihydromorphinone, acetyl-dihydrocodeinone, dihydromorphine, their esters and the salts of any of these substances and of their esters, morphine-N-oxide (commonly known as genomorphine), the morphine-N-oxide derivatives, and any other pentavalent nitrogen morphine derivatives;
- (h) thebaine and its salts, and (with the exception of methylmorphine, commonly known as codeine, and ethylmorphine, commonly known as dionin, and their respective salts) benzylmorphine and the other ethers of morphine and their respective salts;

†By an Order in Council, S.R. & O., 1933, No. 800, these substances became drugs under Part III of the 1920 Act, but are not subject to the regulations which apply to the other drugs in that part. They are subject to special regulations, viz., The Methylmorphine and Ethylmorphine Regulations, 1933 (see page 1145).

- (i) any preparation, admixture, extract or other substance containing any proportion of any of the substances mentioned in paragraph (g) or in paragraph (h) of this sub-section.

For the purpose of the foregoing provision the expression "ecgonine" means lævo-ecgonine, and includes any derivatives of ecgonine from which it may be recovered industrially, and the percentage in the case of morphine shall be calculated as in respect of anhydrous morphine.

*Sub-section 2.*—By Order in Council this part of the Act may be applied to new derivatives of morphine, cocaine, or any other substance.

#### **PART IV.—General. Section 9.—Application of Customs Acts.**

*Section 10. Sub-section 1.*—A constable or person authorised by a Secretary of State has power to inspect books or documents relating to dealings and stocks. *Sub-section 2.*—Any person delaying, or obstructing, or failing to produce, or concealing, or attempting to conceal books, stocks, drugs or documents shall be guilty of an offence.

*Section 11.*—Every regulation made under the Act is to be laid before Parliament.

*Section 12.*—The Secretary of State is empowered to grant licences or authorities on such terms and subject to such conditions, including the payment of a licence fee, as he thinks fit.

*Section 13.*—Heavy fines with or without imprisonment for offences under the Act. If any person attempts to commit an offence, or solicits or incites another person to commit it, he shall, without prejudice to any other liability, be liable on summary conviction to the same punishment and forfeiture as if he had committed it. Where a person convicted of an offence is a company, the chairman and every director and every officer concerned in the management of the company shall be guilty of the like offence unless he proves that the act constituting the offence took place without his knowledge or consent.

*Section 14.*—Permits any constable to arrest without warrant in certain circumstances.

*Section 15.*—Interpretation section, and includes the following definitions:—**"Raw Opium"** includes powdered or granulated opium, but does not include medicinal opium.

**"Prepared Opium"** means opium prepared for smoking, and includes dross and any other residues remaining after opium has been smoked.

**"Medicinal Opium"** means raw opium which has undergone the processes necessary to adapt it for medicinal use in accordance with the requirements of the *British Pharmacopœia*, whether it is in the form of powder or is granulated, or is in any other form, and whether it is or is not mixed with neutral substances.

*Section 16.*—Application to Ireland.

### **DANGEROUS DRUGS AND POISONS (AMENDMENT) ACT, 1923, SUMMARISED.**

(13 AND 14 GEO. V, CHAPTER 5.)

*This Act amends, by deletion, addition or substitution, certain of the sections of the Dangerous Drugs Act, 1920. The amendments have been incorporated in our notes on that Act. The only entirely new provision is contained in Section 5, which relates to the calculation of percentages in the case of liquid preparations, and, as amended by the Pharmacy and Poisons Act, 1933, is as follows:—*

*Section 5.*—For the purposes of Section 8 of the Dangerous Drugs Act, 1920, percentages, in the case of liquid preparations, shall, unless other provision in that behalf is made by regulations under those Acts respectively, be calculated on the basis that a preparation containing one per cent. of any substance means a preparation in which one gramme of the substance, if a solid, or one millilitre of the substance, if a liquid, is contained in every one hundred millilitres of the preparation, and so in proportion for any greater or less percentage.

### **DANGEROUS DRUGS ACT, 1925, SUMMARISED.**

(15 AND 16 GEO. V, CHAPTER 74.)

*This Act amends, by deletion, addition or substitution, certain of the sections of the Dangerous Drugs Act, 1920, and the Dangerous Drugs and Poisons (Amendment) Act, 1923. The amendments have been incorporated in our notes on those Acts. The only entirely new provisions are contained in Sections 1 (ii) and 5, which respectively define "coca leaves" and "Indian hemp," and provide*



power to exclude certain preparations from Part III of the Dangerous Drugs Act, 1920, and are as follows:—

*Section 1. Sub-section 2.—*

“Coca Leaves” means the leaves of any plant of the genus *Erythroxylaceæ* from which cocaine can be extracted either directly or by chemical transformation.

“Indian hemp” means the dried flowering or fruiting tops of the pistillate plant known as *cannabis sativa* from which the resin has not been extracted, by whatever name such tops are called.

*Section 5.*—If His Majesty in Council thinks fit to declare that a finding with respect to any preparation containing any of the drugs to which Part III of the Dangerous Drugs Act, 1920, as amended by this Act, applies, has in pursuance of Article 8 of the Geneva Convention been communicated by the Council of the League of Nations to the parties of the said Convention, the provisions of the said Part III shall as from such date as may be specified in the Declaration cease to apply to the preparation specified therein.

### DANGEROUS DRUGS ACT, 1932, SUMMARISED.

(22 GEO. V, CHAPTER 15.)

*This Act amends, by deletion, addition or substitution, certain of the sections of the Dangerous Drugs Act, 1920 to 1925. The amendments have been incorporated in our notes on those Acts.*

*The only entirely new provisions are contained in Sections 2 and 4, which respectively provide for the prohibition of trade, etc., in new drugs, including power to apply Part III of the Dangerous Drugs Act, 1920 (described as the principal Act) with or without modifications to certain drugs, and provide power to alter or revoke Orders or Declarations in Council, and are as follows:—*

*Section 2.*—(1) It shall not be lawful for any person in the United Kingdom to trade in or manufacture for the purpose of trade any products obtained from any of the phenanthrene alkaloids of opium or from the egonine alkaloids of the coca leaf, not being a product which was on the thirteenth day of July, nineteen hundred and thirty-one, being used for medical or scientific purposes:

Provided that if His Majesty is at any time satisfied as respects any such product that it is of medical or scientific value, he may by Order in Council direct that this sub-section shall cease to apply to that product.

If any person acts in contravention of this sub-section, he shall be guilty of an offence against the principal Act.

(2) If it is made to appear to His Majesty that a decision with respect to any such product as is mentioned in sub-section (1) of this section has in pursuance of Article II of the Geneva Convention (No. 2) been communicated by the Secretary-General of the League of Nations to the parties to the said Convention, His Majesty, by Order in Council, may, as the case requires, either declare that the provisions of the said Part III shall apply to that product in the same manner as they apply to the drugs mentioned in sub-section (1) of section eight of the principal Act as amended by this Act or apply the said Part III to that product with such modifications as may be specified in the Order.

(3) His Majesty may by Order in Council apply Part III of the principal Act, with such modifications as may be specified in the Order, to any of the following drugs, that is to say, methylmorphine (commonly known as codeine), ethylmorphine (commonly known as dionin) and their respective salts.

*Section 4.*—An Order or Declaration made by His Majesty in Council under the Dangerous Drugs Acts, 1920 to 1932, may be varied or revoked by a subsequent Order or Declaration made in the like manner and subject to the like provisions.

### DANGEROUS DRUGS REGULATIONS, 1937 SUMMARISED

MADE IN PURSUANCE OF SECTION 7 OF THE DANGEROUS DRUGS ACT, 1920.

**REGULATION 1. Manufacture.**—Prohibited except by an authorised person on authorised premises and in accord with the terms and conditions of his authority.

**2. Supply, procuring and advertising.**—Prohibited except by an authorised person and in accord with the terms and conditions of his authority.

The administration of a drug, etc., by or under the direct personal supervision, and in the presence of a doctor (or dentist for dental treatment) is not deemed supplying.

**3. Possession.**—Prohibited unless authorised. A person to whom a drug, etc., is lawfully supplied by a doctor or veterinary surgeon who dispenses his own medicines, or on a prescription given by a doctor, dentist or veterinary surgeon is authorised to be in possession, provided that he is not obtaining drugs, etc., from another doctor unknown to the first. A person is deemed to have possession if the drug is in his actual custody or is held for him by any other person.

**4. Delivery to messengers.**—Where a drug is to be supplied to a recipient otherwise than by a doctor or on a doctor's prescription, the supplier may only give it to a messenger sent by the recipient if that messenger is an authorised person or if he produces a written statement signed by the recipient to the effect that he is authorised to receive the drug on the latter's behalf. Such a messenger is an authorised person for such period only as suffices for delivery.

**5. General authority.**—(a) Medical practitioners, (b) dentists, (c) veterinary surgeons, (d) pharmacists dispensing at public hospitals or institutions, (e) persons in charge of a laboratory used for research or instruction and attached to a university, university college, public hospital or other institution approved by the Secretary of State, (see Dangerous Drugs (Approved Institutions) Orders, No. 20 and 22), (f) persons appointed by a local authority as analysts of food and drugs under the Food and Drugs (Adulteration) Act, 1928, (g) persons acting as sampling officers under the Food and Drugs (Adulteration) Act, 1928, (h) inspectors appointed by the Pharmaceutical Society under the Pharmacy and Poisons Act, 1933, (i) persons employed or engaged in testing the quality and amount of drugs, preparations and appliances supplied under the National Health Insurance Acts 1936-1937, and the regulations made thereunder, are authorised, so far as may be necessary for their professions or employments, as members of their respective classes, to be in possession of and to supply the drugs, except that a dentist may not supply drugs, etc., unless they are administered by, or under his direct supervision and in his presence to persons receiving treatment from him.

**6.** (i) Persons who are authorised sellers of poisons within the meaning of the Pharmacy and Poisons Act, 1933, are authorised (a) to manufacture on the registered premises in the ordinary course of their retail business (i) any extract or tincture of Indian Hemp and (ii) any preparation; and (b) subject to the provisions of the Regulations, to carry on on the registered premises the business of retailing, dispensing or compounding drugs, etc.

(ii) Every drug, etc., in the actual custody of a person authorised by this Regulation shall be kept in a locked receptacle which can be opened only by him or some assistant of his being a pharmacist.

**7. Withdrawal of authority.**—The Secretary of State is empowered to withdraw the authority from authorised persons convicted of offences against the Act. If the person is authorised by virtue of the preceding Regulation, the Council of the Pharmaceutical Society of Great Britain must be first consulted. If he is a doctor, dentist, or veterinary surgeon, the Secretary of State may direct that it shall be unlawful for that person to give prescriptions. If the Secretary of State suspects that a doctor or dentist is using, supplying or prescribing drugs otherwise than properly required for medical or dental treatment, he may refer the matter to a tribunal constituted as stated in the First Schedule to these Regulations, and on its recommendation, withdraw the person's authority.

**8. Prescriptions.** (1) A prescription means a prescription directing the supply of a drug, and given either by a medical practitioner for medical treatment, by a dentist for dental treatment, or by a veterinary surgeon for animal treatment. (2) The prescription must (a) be in writing and be signed by the person giving it with his usual signature and be dated by him, and (b) except in a health insurance prescription, specify the address of the person giving it, (c) specify the name and address of the person for whose treatment it is given, or, if it is given by a veterinary surgeon, of the person to whom the article prescribed is to be delivered, (d) have written thereon, if given by a dentist, the words "For local dental treatment only," and, if given by a veterinary surgeon, the words "For animal treatment only," (e) specify, if it prescribes a preparation contained, or compounded of preparations all of which are contained in the B.P., the B.P.C., or the N.H.I. Drug Tariff, the total amount of the preparation, or of each preparation, as the case may be, and in any other case the total amount of the drug to be supplied.

**9. Dispensing of prescriptions.**—(1) A person shall not supply a drug on a prescription (a) unless the prescription complies with the above, and (b) unless in the case of a health insurance prescription he has no reason to suppose that it is not genuine, or, in the case of any other prescription, he either (i) is acquainted

with the signature of the person by whom it purports to have been given, and has no reason to suppose that it is not genuine, or (ii) has taken reasonably sufficient steps to satisfy himself that it is genuine. (2) If a prescription expressly states that it may, subject to the lapse of a specified interval or intervals, be dispensed two or three times, the drug may be supplied a second or third time after the specified interval or intervals and no more, but otherwise a prescription shall not be taken to authorise the drug to be supplied more than once. (3) The person dispensing shall, at the time, mark on the prescription the date on which it is dispensed, and, in the case of a prescription which may be dispensed two or three times, the dates of the second and third time, and, unless it is a health insurance prescription, retain it and keep it on the premises to be available for inspection.

**10. Marking of packages or bottles.**—(1) No person shall (a) supply a drug unless the package or bottle is marked with the amount contained, or (b) supply a preparation, unless the package or bottle is plainly marked (i) in the case of a powder, solution, or ointment, with the total amount contained and the percentage of the drug contained, or (ii) in the case of tablets or other similar articles, with the amount of the drug in each article and the number of articles contained. (2) This does not apply to a prescription lawfully given by a medical practitioner.

**11. Records.**—(1) Every person authorised to supply shall (a) keep a register as set out as in the Second Schedule to these Regulations and enter therein true particulars as to every quantity of drug or preparation obtained by him and supplied by him, whether to persons within or without Great Britain, (b) use a separate register or separate part of the register for each of the various classes of drugs and preparations, (c) make the entry on the day on which the drug is received, or on which the transaction takes place, or, if that is not practicable, on the following day, (d) keep a separate register in respect of each set of business premises (subject to the approval of the Secretary of State, an authorised person may keep a separate register for each department of the business), (e) make no cancellation, obliteration, or alteration (any correction of an entry must be made by way of a marginal or foot note giving the date of correction), (f) on demand by the Secretary of State or by a person authorised in writing by him, furnish particulars required as to the obtaining or supplying or as to stocks, (g) the register may be used for entries required under Section 18 (2) (b) of the Pharmacy and Poisons Act, 1933, but, save as aforesaid, not for any other purpose. (2) The entering in the register shall not apply to (a) a medical practitioner who enters in a day book particulars of every drug or preparation supplied by him to any person, with the name and address of that person, and the date of supply, and enters in a separate book kept for the purposes of the Regulation a reference to each entry in the day book which relates to the supply, or (b) an authorised seller of poisons within the meaning of the Pharmacy and Poisons Act, 1933, who enters in a separate book kept for the purposes of this Regulation a proper reference to each entry in a Pharmacy Act book which relates to the supply of any drug or preparation. (3) References in the separate book must be made in chronological order, and the book must be kept in separate parts relating respectively to each of the several classes of drugs, and must not be used for any other purpose. (4) The entry in the day book or separate book must be made on the day an entry would have been required to be made in the register. (5) Every register, separate book, or day book in which any entry with respect to the supply of a drug or preparation is made, and every Pharmacy Act book containing an entry referred to in the separate book shall be kept on the premises to which the register or book relates or where the prescription was dispensed, so as to be available at all times for inspection. (6) Every entry and every correction must be made in ink, or indelibly written. (7) In this Regulation (i) a drug or preparation administered by, or under the direct supervision and in the presence of a medical practitioner or a dentist, shall not be deemed to have been supplied by him; (ii) a "proper reference" means a reference entered in the separate book under the same date as the entry in the day book or Pharmacy Act book, and otherwise such as to enable the entry to be easily identified.

**12. Export.**—Any drugs exported from a foreign country to another foreign country and brought into the U.K. must not, unless it is authorised by the Secretary of State, be diverted to any destination other than that stated in the authority for export from the country of export.

**13. Special provisions for ships, farmers, stockowners and midwives.**—The master of a ship not carrying a doctor may, subject to certain conditions, supply drugs to members of the crew providing a complete entry

specifying the drug used is made in the log-book. The M.O.H. or assistant M.O.H. of a port may issue a certificate to the master of a foreign ship authorising him to purchase and possess such quantity of drugs as he considers necessary until the ship reaches its home port. A person who supplies drugs on such a certificate shall retain it and mark it with the date on which the drug was supplied and keep it on his premises for inspection.

Farmers and stockowners who have obtained a certificate as set out in the Third Schedule to the Regulations from the Chief Officer of Police for the area in which they carry on business are authorised to be in possession of tincture of opium *B.P.*, for use solely in the treatment of animals, subject to the conditions specified in the certificate.

Certified and practising midwives are authorised to be in possession of and to administer preparations of opium so far as is necessary for the practice of their profession. They must enter in a book kept solely for this purpose particulars of all supplies obtained, including the date on which, and the name and address of the person from whom, the supply was obtained, and the quantity obtained.

**14. Preservation of documents.**—All records, prescriptions, etc., must be kept for two years from the date of the last entry or the date of issue, as the case may be.

**15.**—The Secretary of State may, subject to any conditions he may prescribe, exempt any hospital or other public institution from any provision of these Regulations.

**16. Exemption of certain drugs and prescriptions.**—The following are exempted from the conditions of these Regulations—(a) any drug, etc., mentioned in the Fourth Schedule to these Regulations or a drug, etc., which has been denatured as approved by the Secretary of State; (b) (i) any prescription issued for the purpose of testing the quality and amount of drugs, preparations and appliances supplied under the N.H.I. Acts, and the Regulations made thereunder, (ii) any prescription issued to a sampling officer under the Food and Drugs (Adulteration) Act, 1928.

**17. Interpretation.**—Includes the following definitions:—

**Drug.**—Any drug not being a preparation within the meaning of these Regulations to which Part III of the 1920 Act applies.

**Registered Premises.**—Premises registered under Part I of the Pharmacy and Poisons Act, 1933.

**Pharmacy Act Book.**—Either of the books required to be kept under Sections 18 (2) and 19 (3) of the Pharmacy and Poisons Act, 1933.

**Register.**—A bound book and not a loose-leaf register or card index.

In addition (a) a person authorised to manufacture shall be deemed authorised to supply, and (b) a person authorised to supply shall be deemed to be a person authorised to be in possession of, to procure, to offer to supply or procure, and to advertise for sale.

## FIRST SCHEDULE.

*Constitution of Reference Tribunal for the purpose of Regulation 7, (3).*

## SECOND SCHEDULE.

### FORM OF REGISTER.

#### PART I.—*Drugs or preparations obtained.*

(The class of drugs and preparations to be specified at the head of each page.)

Date on which received.	Name.	Address.	Amount obtained.	Form in which obtained.
	of person or firm from whom obtained.			

PART II.—*Drugs or preparations supplied.*

(The class of drugs and preparations to be specified at the head of each page.)

Date of trans- action.	Name.	Address.	Authority of person or firm supplied to be in possession.	Amount supplied.	Form in which supplied.
	of person or firm supplied.				

## THIRD SCHEDULE.

*Certificate authorising farmers and stockowners to purchase tincture of opium, B.P.*

## FOURTH SCHEDULE.

*Drugs and Preparations exempted from these Regulations.*

Pasta Arsenicalis, *B.P.C.* 1934.  
 Pil. Ipecac. c. Scilla, *B.P.C.* 1934.  
 Pil. Digitalis et Opii Co., *B.P.C.* 1923.  
 Pil. Hydrarg. c. Cret. et Opii, *B.P.C.* 1934.  
 Pulv. Cretæ Aromat. c. Opio, *B.P.* 1932.  
 Pulv. Ipecac. et Opii, *B.P.* 1932.  
 Suppos. Plumbi c. Opio, *B.P.* 1932.  
 Tabellæ Plumbi c. Opio, *B.P.C.* 1934.  
 Elixir Diamorphinæ et Terpini c. Apomorphina, *B.P.C.* 1934.  
 Linctus Diamorphinæ Camphoratus, *B.P.C.* 1923 and 1934.  
 Linctus Diamorphinæ c. Ipecacuanha, *B.P.C.* 1934.  
 Linctus Diamorphinæ et Scillæ, *B.P.C.* 1923 and 1934.  
 Linctus Diamorphinæ et Thymi, *B.P.C.* 1923 and 1934.  
 Mixtures of Pulv. Ipecac. et Opii, *B.P.* 1932 with any of the following:—  
     Hydrarg. c. Cret., *B.P.* 1914 and 1932.  
     Acetylsalicylic Acid.  
     Phenacetin.  
     Quinine and its Salts.  
     Sodium Bicarbonate.

Cocaine Eyedrops—a preparation consisting of an admixture of cocaine in castor oil with mercuric chloride in a proportion of not more than one part in 200 of cocaine and not less than one part in 3000 of mercuric chloride.

Methylmorphine and ethylmorphine and their respective salts and any preparation, admixture or other substance containing any proportion of methylmorphine or ethylmorphine associated with an inert substance whether solid or liquid; and preparations and admixtures or other substances containing more than 2.5 per cent. of methylmorphine or ethylmorphine (calculated as pure drug) associated with other medicinal substances.

## ORDERS IN COUNCIL APPLYING TO DANGEROUS DRUGS ACT, 1920, SUMMARISED.

**1. Methylmorphine and Ethylmorphine.** (April 13th, 1937). Brings any preparation, admixture or other substance (except Syrupus Codeinæ Phosphatis *B.P.C.* 1934) containing any proportion of methylmorphine (commonly known as codeine) or ethylmorphine (commonly known as dionin) associated with any inert substance whether solid or liquid, and any preparation, admixture or other substance containing more than 2.5% of methylmorphine or ethylmorphine (calculated as pure drug) associated with any other medicinal substance into Part III of the 1920 Act. Schedule Four of the Dangerous Drugs Regulations 1937, however, exempts all these preparations, admixtures and substances from the provisions of these regulations. Hence the ultimate effect of the order is to bring the import and export of these substances under control, and in no other way alters the position of codeine and dionin (*see* p. 1145).

**2. Ecgonine and Morphine.** The order of June 8th, 1937, states that after July 1st, 1937, Part III of the 1920 Act shall apply to all preparations of esters of ecgonine or of their respective salts and all preparations of ecgonine containing less than one-tenth per cent. of ecgonine and to all preparations of esters of morphine in the same manner as the said Part III applies to the drugs mentioned in Section 8 (i) of the 1920 Act (*see p.* 1133).

**3. Exemptions.** The order of April 13th, 1937, states that in accordance with Article 8 of the International Opium Convention, Part III of the 1920 Act shall cease to apply to the articles specified in the following schedule after June 30th, 1937.

#### SCHEDULE.

##### (a) Morphine Preparations.

1. *Cereoli iodoformi et morphinæ*.—In 1 bougie, iodoform 0.320 g., morphine hydrochloride 0.016 g., oil of theobroma, sufficient to fill a 1 g. mould.
2. *Emplastrum opii*.—Elemi 20 g., terebinthina 30 g., cera flava 15 g., olibanum pulvis 18 g., benzoes pulvis 10 g., opii pulvis 5 g., balsamum peruvianum 2 g.
3. *Emplastrum opii*.—Extract of opium 25 g., refined elemi 25 g., diachylon plaster with gum 50 g.
4. *Emplastrum opii*.—Elemi 8 g., terebinthinæ communis 15 g., cera flavæ 5 g., olibani pulveratæ 8 g., benzoes pulveratæ 4 g., opii pulverati 2 g., balsami peruviani 1 g.
5. *Emplastrum opii*.—Opium, in very fine powder 10 g., resin plaster 90 g.
6. *Emplastrum opii* (*see formula under 5*) mixed with other plasters contained in the B.P. or B.P.C.
7. *Linimentum opii*.—Tincture of opium 500 ml., liniment of soap, 500 ml.
8. *Linimentum opii* (*see formula under 7*) mixed with any other liniment of the B.P. or of the B.P.C.
9. *Linimentum opii ammoniatum*.—Ammoniated liniment of camphor 30, tincture of opium 30, liniment of belladonna 5, strong solution of ammonia 5, liniment of soap to 100.
10. *Linimentum opii ammoniatum* (*see formula under 9*) mixed with any other B.P. or B.P.C. liniment.
11. *Caustic "Nerve Pastes."*—Preparations containing in addition to morphine salts, or morphine and cocaine salts, at least 25% of arsenious acid, and made up with the requisite proportion of creosote or phenol to produce the consistency of a paste.
12. *Diarrhœa pills*.—Camphor 0.0648 g., lead acetate 0.013 g., bismuth subnitrate 0.162 g., tannic acid 0.0648 g., opium powder 0.026 g.
13. *Pilule digitalis et Opii compositæ*.—Digitalis leaves, in powder 0.31 g., opium in powder 0.19 g., ipecacuanha root, in powder 0.13 g., quinine sulphate 0.78 g., syrup of glucose, a sufficient quantity to make 12 pills.
14. *Pilule hydrargyri cum Opio*.—Mercury pill 3.89 g., opium in powder 0.19 g., to make 12 pills.
15. *Pilule hydrargyri cum Creta et Opii*.—Mercury with chalk 0.78 g., compound powder of ipecacuanha (*see formula under 21*) 0.78 g., milk sugar and syrup of glucose, of each a sufficient quantity to make 12 pills.
16. *Pilule ipecacuanhæ cum Scilla*.—Compound powder of ipecacuanha (*see formula under 21*) 30 g., squill, in powder 10 g., ammoniacum, in powder 10 g., syrup of glucose, a sufficient quantity.
17. *Pilule hydrargyri bichlorati cum Opii extracto*.—Bichloride of mercury triturated 10 cg., extract of opium 20 cg., extract of couch-grass 20 cg., liquorice root in powder, q.s. for 10 pills.
18. *Pilule hydrargyri iodati cum Opii pulvere*.—Hydrargyrum iodatum, freshly prepared 50 cg., opium powder 20 cg., powdered liquorice 30 g., white honey, q.s. for 10 pills.
19. *Pilula plumbi, cum Opio*.—Lead acetate, in powder 80 g., opium, in powder 12 g., syrup of glucose 8 g. (or a sufficient quantity).
20. *Pilule terebinthinæ compositæ*.—Opium 0.5 g., chinini sulfas 2 g., styrax liquidus 2 g., terebinthina laricina 8 g., magnesi subcarbonas, a sufficient quantity to make 100 pills.
21. *Pulvis ipecacuanhæ compositus*. *Syn.* PULVIS IPECACUANHÆ ET OPII, DOVER'S POWDER. Ipecacuanha root, in powder 10 g., opium, in powder 10 g., potassium sulphate in powder 80 g.
22. Mixtures of *Dover's powder* (*see formula under 21*) with mercury and chalk, aspirin, phenacetin, quinine and its salts, and sodium bicarbonate.

23. *Pulvis kino compositus*.—Kino, in powder 75 g., opium, in powder 5 g. cinnamon bark, in powder, 20 g.

24. *Suppositoria plumbi composita*. *Syn.* SUPPOSITORIA PLUMBI CUM OPIO. Lead acetate, in powder 2.4 g., opium, in powder 0.8 g., oil of theobroma, a sufficient quantity for 12 suppositories, each weighing about 1 g.

25. *Coryza Tablets No. 2*.—Powdered opium 0.0043 g., quinine sulph. 0.022 g., ammon. chlor. 0.022 g., camphor 0.022 g., ext. belladonna leaves 0.0043 g., ext. aconite root 0.0043 g.

26. *Diarrhoea Tablets No. 2*.—Powdered opium 0.016 g., camphor 0.016 g., powdered ipecacuanha 0.008 g., lead acetate 0.011 g.

27. *Dysentery Tablets*.—Powdered opium 0.013 g., powdered ipecacuanha 0.0648 g., powdered calomel 0.0324 g., lead acetate 0.0324 g., bismuth betanaphthol 0.1944 g.

28. *Tabella hydrargyri cum Opio*.—Mercurous chloride powder 0.065 g., antimony oxide powder 0.065 g., ipecacuanha-root powder 0.065 g., powdered opium 0.065 g., milk sugar 0.065 g., gelatine solution, a sufficient quantity to make 1 tablet.

29. *Tabella plumbi cum Opio*.—Sugar of lead 0.195 g., powdered opium 0.065 g., gelatine solution, a sufficient quantity to make 1 tablet.

30. *Tabletæ plumbi cum Opio*.—Lead acetate, in fine powder 19.44 g., opium, in powder 3.24 g., refined sugar, in powder 6.48 g., ethereal solution of theobroma 3.60 ml., alcohol 0.90 ml.

31. *Unguentum gallæ compositum*.—Galls in very fine powder 20, extract of opium 4, distilled water 16, wool fat 10, soft paraffin, yellow 50.

32. *Unguentum gallæ compositum* (see formula under 31) mixed with other ointments and plasters contained in the B.P. or B.P.C.

33. *Unguentum gallæ cum Opio*.—Gall ointment 92.5 g., opium in powder 7.5 g.

34. *Unguentum gallæ cum Opio* (see formula under 33) mixed with other ointments and plasters contained in the B.P. or B.P.C.

35. *Yatren*—105 (iodoxyquinoline-sulphonic acid) with 5% opium admixture.

#### (b) Cocaine Preparations.

1. *Bernatzik's Injections*.—(a) Hydrargyrum bicianatum 0.03 g., cocainum 0.02 g., (b) Hydrargyrum succinatum 0.03 g., cocainum 0.01 g.

2. *Stila's Injections*.—(a) Hydrargyrum succinatum 0.03 g., cocainum muriaticum 0.01 g., (b) Hydrargyrum succinatum 0.05 g., cocainum muriaticum 0.03 g.

3. *Natrium biboracicum compositum cum cocaino*.—In tablets, compressed tablets, lozenges, pastilles and the like, difficult to break up, and containing not more than 0.2% of cocaine salts in conjunction with not less than 20% borax and not less than 20% antipyrine, or some similar analgesic, and not more than 40% of flavouring matter. Maximum weight of each tablet, etc., 1 g.

4. *Caustic "Nerve Pastes"*.—Preparations containing, in addition to cocaine salts or cocaine and morphine salts, at least 25% of arsenious acid, and made up with the requisite proportion of creosote or phenol to produce the consistency of a paste.

5. *Cocaine and atropine tablets*, with a content of not more than 0.0003 g. of cocaine salts and not less than 0.0003 g. of atropine salts to each tablet. Atropinum sulphuricum 0.0003 g., cocainum hydrochloricum 0.0003 g., mannite 0.003 g. Weight of one tablet 0.0036 g. Cocaine content 8.3%.

#### (c) Heroin Preparations.

1. *Elixir camphoræ compositum*.—Camphor 4 gr., oil of anise 5 m., benzoic acid 6 gr., diamorphine hydrochloride 4 gr., liquid extract of ipecacuanha 120 m., tincture of squill 1½ fl. oz., simple syrup to 20 fl. oz.

2. *Elixir diamorphine et terpin*, with *apomorphine*.—Apomorphine hydrochloride 5 gr., diamorphine hydrochloride 4 gr., terpin hydrate 44 gr., alcohol 10 fl. oz., glycerine 5 fl. oz., syrup of wild cherry to 20 fl. oz.

3. *Linctus diamorphine with ipecacuanha*.—Liquid extract of ipecacuanha 120 m., diamorphine hydrochloride 4 gr., tincture of hyoscyamus 1½ fl. oz., spirit of chloroform 1½ fl. oz., syrup of balsam of tolu 3 fl. oz., syrup of wild cherry 3 fl. oz., glycerine to 20 fl. oz.

4. *Linctus senegæ compositus*.—Liquid extract of senega 1 fl. oz., liquid extract of squill 1 fl. oz., tartarated antimony 8 gr., diamorphine hydrochloride 4 gr., glycerine 2 fl. oz., simple syrup to 20 fl. oz.

5. *Linctus thymi compositus*.—Diamorphine hydrochloride 4 gr., apomorphine hydrochloride 5 gr., distilled water 1 fl. oz., liquid extract of thyme (1-1) 5 fl. oz., solution of tolu  $1\frac{1}{2}$  fl. oz., glycerine to 20 fl. oz.

(d) **Dicodide Preparations.**

1. *Cardiazol-Dicodide Solutions*.—Solutions containing not less than 10% of cardiazol and not more than 0.5% of dicodide salts.

(e) **Eucodal Preparations.**

1. *Anti-Opium Tablets*.—Eucodal 1 g., pulvis gentianæ 35 g., pulvis ipecacuanhæ 20 g., quinine sulphate 20 g., caffeine 5 g., sugar of milk 25 g., mix up and make up 5 gr. tablets.

In exempting this preparation from the operation of the Geneva Convention, the Health Committee expressed the wish that it should not be offered to the public under the name of "anti-opium."

2. *Tablets B.B. Compound*.—Berberis vulgaris powder 0.0324 g., nux vomica 0.013 g., eucodal 0.0032 g., ipecacuanha 0.0648 g., rhubarb 0.013 g., pulvis cinnamoni compositus 0.0324 g., aromatic chalk 0.0032 g.

### DANGEROUS DRUGS (HOSPITAL GENERAL EXEMPTION) ORDER (1924), SUMMARISED.

By Order dated August 9, 1924, certain hospitals and other institutions are exempted from operation of the Regulations on compliance with certain conditions. This Order substitutes and revokes an Order on the same subject made August 15, 1921. Exempted are:—Any hospital or infirmary, asylum, poor-law institution or sanatorium supported by any public authority, or out of public funds or by a charity or voluntary subscription, in which the drugs are dispensed by a medical practitioner or a pharmacist or—in a poor-law institution—a dispenser whose qualifications and appointment are approved by the Minister of Health, if the conditions of Schedule I (below) are complied with, or, if there is no such dispenser, if the conditions of Schedule II (below) are complied with. Any institution exempted under this Order may be inspected at any time by any person so authorised by the Secretary of State, to ensure that the prescribed conditions are being fulfilled.

#### SCHEDULE I.

1. Orders for supplies must be signed by the pharmacist, or if no such person is employed, by one of the medical practitioners attached to the hospital.
2. Supplies to be kept in the charge of the person responsible for dispensing, and records to be kept.
3. The medicine only to be dispensed for use of an individual patient, etc.
4. The person responsible for dispensing the drugs shall at the time of dispensing any prescription stamp, or otherwise mark, the prescription with the prescribed particulars, and shall keep records.
5. Prescriptions must be kept for two years.
6. Stock preparations in wards or out-patient department shall only be supplied on the requisition of the sister in charge, who shall keep the drugs under lock and key, and only be used by her in accordance with the directions of one of the medical practitioners in charge of the patients.
7. A requisition shall be marked in the dispensary to show that it has been complied with, filed there, and a copy or note of the requisition kept by the sister in charge.
8. Precautions shall be taken to prevent any theft of the drugs.
9. Preparations may be prescribed by any name known in the hospital.
10. Nothing in this Schedule shall affect any medicine or other substance to which the Regulations do not apply.

#### SCHEDULE II.

Supplies are to be to, or on the order of, a medical practitioner attached to the hospital (not the dispenser), and he must certify that the supply is necessary for the treatment of the patients. The matron is to be responsible for keeping the drugs (in a locked cupboard, of which she alone shall have the key), and for using or administering them and recording their purchase, but they are only to be used, etc., under the direction of a medical practitioner attached to the hospital. Except so far as this Schedule modifies them, the Regulations must be observed—for instance, the chemist supplying a hospital must record the supplies, get them signed for and mark the packages as on ordinary sales.



### DANGEROUS DRUGS (HOSPITAL GENERAL EXEMPTION) (AMENDMENT) ORDER, 1939, SUMMARISED.

(1) Drugs kept at a hospital or other institution to which this Order applies may, during a period of emergency, be distributed, in accordance with arrangements made by the Minister of Health, by the person responsible for dispensing medicines at the hospital or other institutions to a hospital included in the Emergency Hospitals Scheme or first-aid post established for the treatment of persons injured in a hostile attack. The said person must record the name and address of the hospital included in the Emergency Hospital Scheme or first-aid post to which the drug is distributed, the quantity of the drug distributed, the date of distribution, and the person to whom it is delivered for conveyance to the hospital or first-aid post.

(2) This Order applies to any hospital, infirmary, mental hospital, asylum, Poor Law institution or sanatorium supported by any public authority or out of any public funds or by a charity or voluntary subscriptions, in which the drugs dispensed by a doctor or pharmacist or, in the case of a Poor Law institution, by a dispenser whose qualifications and appointment are approved by the Minister of Health, if the conditions of the first schedule to the Dangerous Drugs (Hospital General Exemption) Order, 1924, are complied with.

### NURSING HOMES.

The Dangerous Drugs (Hospital General Exemption) Order (1924) does not apply to nursing homes, and drugs to which the Dangerous Drugs Acts and Regulations apply may only be supplied for the use of patients in like manner as the drugs may be supplied to patients in their own homes. A separate prescription must be written by the medical practitioner for the individual patient. The nursing home may not hold a "stock" of drugs. For a note of the conditions under which poisons other than "dangerous drugs" may be supplied to nursing homes to hold as a "stock," see page 1107.

### SPECIAL AUTHORISATIONS.

Although persons within the classes indicated below may be supplied with the preparations mentioned, they must comply with the special conditions laid down for each by the Home Office.

In supplying the drugs to the authorised persons the full requirements of the Dangerous Drugs Acts and Regulations, and of the Pharmacy and Poisons Act and Rules, must be observed.

#### Cocaine in Castor Oil to Owners of British Steam Fishing Vessels. (Dec. 1927.)

Eye-drops of the same formula as that indicated for supply to factory owners may be sold to the owner of a British steam fishing vessel. For conditions of authority of masters of British or foreign ships (other than British steam fishing vessels) to be in possession of certain drugs, see Regulation 13 of the Dangerous Drugs Regulations, 1937, page 1137.

#### Agents of Overseas Governments. (Dec. 1933.)

Certain persons named in the Schedule to the authorisation may procure "dangerous drugs" for their respective governments. The drugs must be obtained from persons or firms licensed to supply them. The persons named are *not* authorised to be in possession of the drugs.

### RAW OPIUM, ETC., REGULATIONS, 1937, SUMMARISED.

MADE UNDER SECTION 3 OF THE DANGEROUS DRUGS ACT, 1920, AND SECTION 1 OF THE DANGEROUS DRUGS ACT, 1925.

1. **Supply, procuring and advertising.**—Prohibited, except by an authorised person in accordance with the terms of his authority.

2. **Possession.**—Only authorised persons may be in possession of a drug, *i.e.*, in his actual custody or held by any other person subject to his control or for him or on his behalf.

3. **Delivery to messengers.**—Where a drug is to be supplied to a recipient, the supplier may only give it to a messenger sent by the recipient if that messenger is an authorised person or if he produces a written statement signed by the recipient to the effect that he is authorised to receive the drug on the latter's

behalf. Such a messenger is an authorised person for such period only as suffices for delivery.

**4. General Authority.**—(a) Medical practitioners, (b) veterinary surgeons, (c) authorised sellers of poisons within the Pharmacy and Poisons Act, 1933, (d) pharmacists employed as dispensers at public hospitals or institutions, (e) persons in charge of a laboratory used for research or instruction and attached to a university, university college, public hospital or other institution approved by the Secretary of State, (f) persons appointed by a local authority as analysts under Section 15 of the Food and Drugs (Adulteration) Act, 1928, (g) persons acting as sampling officers under the Food and Drugs (Adulteration) Act, 1928, (h) persons appointed by the Pharmaceutical Society of Great Britain as inspectors under Section 25 of the Pharmacy and Poisons Act, 1933, are authorised as far as may be necessary for the practice of their professions or employment as members of their classes, to be in possession of and supply drugs.

**5. Withdrawal of authority.**—The Secretary of State is empowered to withdraw the authority from any authorised person convicted of an offence against the 1920 Act or under the enactments relating to the Customs as applied by the 1920 Act.

**6. Records.**—Persons authorised to supply drugs shall keep a record as set out in First Schedule to the Regulations and enter in it all transactions. Separate registers or parts of the register must be kept for raw opium, coca leaves and Indian hemp, including resins obtained from Indian hemp and all preparations, except extract or tincture of Indian hemp, of which such resins form the base. Every entry must be made in ink or indelibly on the day on which the transaction takes place, or on the following day. Corrections must be made by means of a marginal or foot-note only, and dated. Separate registers must be kept for each set of premises, or subject to the approval of the Secretary of State for each department of the business. The register must be kept in some part of the premises to which it relates so as to be available at all times for inspection. The authorised person must, on demand, furnish particulars of all transactions and of stocks of drugs held to the Secretary of State or any person empowered in writing by the Secretary of State.

**7. Export.**—Any drugs exported from a foreign country to another foreign country and brought into the U.K. must not, unless it is authorised by the Secretary of State, be diverted to any destination other than that stated in the authority for export from the country of export.

**8. Preservation of documents.**—All registers, records, etc., must be kept for two years from the date of the last entry, and any other documents for two years from the date of issue.

**9. Interpretation.**—Includes the following definition:—

**Drug.**—Any drug, resin or preparation, other than extract or tincture of Indian hemp, to which Part I of the 1920 Act applies.

## FIRST SCHEDULE

### FORM OF REGISTER.

#### PART I.

*Entries to be made in case of drugs obtained.*

(The kind of drug to which the entries relate to be specified at the head of each page in the Register.)

Date on which supply received.	Name	Address	Amount obtained.
	of person or firm from whom obtained.		

## PART II.

*Entries to be made in case of drugs supplied.*

(The kind of drug to which the entries relate to be specified at the head of each page in the Register.)

Date on which the transaction was effected.	Name	Address	Authority of person or firm to whom drug supplied to be in possession thereof	Amount supplied.
	of person or firm to whom supplied.			

### METHYLMORPHINE AND ETHYLMORPHINE REGULATIONS SUMMARISED.

MADE UNDER SECTION 7 OF THE 1920 ACT, AND SECTION 2 (3) OF THE DANGEROUS DRUGS ACT, 1932, FOR CONTROLLING THE MANUFACTURE, SALE, POSSESSION AND DISTRIBUTION OF METHYLMORPHINE (COMMONLY KNOWN AS CODEINE), ETHYLMORPHINE (COMMONLY KNOWN AS DIONIN) AND THEIR RESPECTIVE SALTS.—S.R. & O., Sept. 13, 1933.

**REGULATION 1. Manufacture.**—Prohibited, except by a licensed person and in accord with the terms and conditions of his licence.

**2. Supply of drugs.**—Except as provided, a wholesale druggist shall not supply a drug to any person either in Great Britain or elsewhere (a) unless licensed, (b) otherwise than in accord with the terms and conditions of his licence, (c) if the drug is to be supplied in any one transaction in quantity exceeding one pound avoirdupois, unless the person to whom it is to be supplied is licensed to be in possession of the drug.

**3. Possession.**—(1) A person shall not be in possession of a drug in a quantity exceeding one pound avoirdupois unless he is so licensed.

(2) A person shall be deemed to be in possession if the drug is in his actual custody, or is held by any other person subject to his control or for him or on his behalf.

**4. Marking of packages or bottles.**—No wholesale druggist licensed to supply a drug shall supply it unless the container is plainly marked with the amount of the drug contained therein.

**5. Keeping of registers.**—Every wholesale druggist licensed to supply shall (a) keep a register, and set out as in the Schedule to these Regulations true particulars as to every quantity of drug obtained by him and supplied by him, whether to persons within or without Great Britain, (b) use a separate register or separate part of the register for (i) methyilmorphine and its salts, (ii) ethylmorphine and its salts, (c) make the entry on the day on which the drug is received or on which the transaction takes place, or, if that is not practicable, on the following day, (d) keep a separate register in respect of each set of business premises (subject to the approval of the Secretary of State, a licensed wholesale druggist may keep a separate register for each department of the business), (e) make no cancellation, obliteration, or alteration (any correction of an entry must be made by way of a marginal or foot note, giving the date of correction), (f) on demand by the Secretary of State, or by a person authorised in writing by him, furnish particulars as to the obtaining or supplying, or as to stocks, (g) the register may be used for entries required under the Pharmacy and Poisons Acts, 1852-1933, but, save as aforesaid, not for any other purpose, (h) every register shall be kept on the premises to which it relates, and so as to be at all times available for inspection.

**6. Preservation of registers.**—All registers which are kept in pursuance of the requirements of these Regulations are to be kept for a period of two years from the date of the last entry.

7. **Regulations not to apply to certain types of sale.**—Nothing in these Regulations shall apply to any sale or distribution of any of the drugs by a person other than a wholesale druggist, nor to any sale or distribution by an authorised seller of poisons in the course of any retail business.

8. **Interpretation.**—(1) In these Regulations the following expressions have the meanings hereby assigned to them:—

"Licence" means any licence issued by the Secretary of State under Section 12 of the Dangerous Drugs Act, 1920, and the expression "licensed" shall be construed accordingly.

"Authorised seller of poisons" means a person lawfully carrying on business in accordance with the provisions of the Pharmacy and Poisons Act, 1933, as an authorised seller of poisons.

"Drug" means Methymorphine, Ethylmorphine and their respective salts.

"Retail business" means the business of retailing or dispensing (or compounding) drugs carried on at a shop.

"Wholesale druggist" means a person who carries on the business of selling drugs to persons who buy to sell again.

(2) For the purpose of these Regulations, but subject to any limitation attached to his licence: (a) a wholesale druggist licensed to manufacture a drug shall be deemed licensed to supply; and (b) a wholesale druggist licensed to supply shall be deemed to be a person licensed to be in possession of that drug for the purpose of Regulation 3 of these Regulations.

### SCHEDULE.

#### FORM OF REGISTER.

##### PART I.—*Drugs obtained.*

(The class of drugs to which the entries relate to be specified at the head of each page in the Register.)

Date on which received.	Name.	Address.	Amount obtained.	Form in which obtained.
	of person from whom obtained.			

##### PART II.—*Drugs supplied.*

(The class of drugs to which the entries relate to be specified at the head of each page in the Register.)

Date of transaction.	Name.	Address.	*Description.	Amount supplied	Form in which supplied.
	of person to whom supplied.				

\*i.e., wholesale druggist, medical practitioner, pharmacist, etc.

**THERAPEUTIC SUBSTANCES ACT, 1925, SUMMARISED.**

(15 AND 16 GEO. V, CHAPTER 60.)

AN ACT TO PROVIDE FOR THE REGULATION OF THE MANUFACTURE, SALE, AND IMPORTATION OF VACCINES, SERA, AND OTHER THERAPEUTIC SUBSTANCES.

1. This Act applies to:—

- (1) Vaccines, sera, toxins, antitoxins and antigens.
  - (2) Salvarsan (dioxo-diamino-arseno-benzol-di-hydrochloride) and analogous substances used for the specific treatment of infective diseases.
  - (3) Preparations of the specific antidiabetic principle of the pancreas known as insulin.
  - (4) Preparations of the posterior lobe of the pituitary body intended for use by injection.
  - (5) Sterilised surgical ligature and sterilised surgical suture (*i.e.*, any ligature or form of binding material prepared from the gut or any tissue of an animal, and offered or intended to be offered for sale as sterile and ready for use in surgical operations upon the human body). (Added S.R. & O. 1931, No. 633.) and any other therapeutic substances, afterwards called "substance," which may from time to time be added by regulations made under this Act as being substances the purity or potency of which cannot be adequately tested by chemical means.
2. (1) To manufacture for sale any substance to which this Act applies licences (personal and premises) from the licensing authority are required.
- (2) The licence continues in force for such period as may be prescribed (two years), but may from time to time be renewed for a like period.
- (3) The conditions under which the substances are manufactured, and the premises, must satisfy the licensing authority.
- (4) A licence may be revoked or suspended if the licensee fails to comply with the requirements.
- (5) This section does not apply to the preparation by a medical practitioner for any of his own patients or for, and at the request of, another practitioner, if specially prepared with reference to the condition, and for the use, of an individual patient.
3. (1) Importation into Great Britain or Northern Ireland necessitates standards of strength, quality and purity, and the substance is to be consigned to a person licensed by the licensing authority to import; or to a person engaged in scientific research holding a special licence to import.
- (3) Substances prohibited come under Section 42 of the Customs Consolidation Act, 1876, and any Act amending or extending.
4. (1) Joint Advisory Committees frame regulations.
5. (1) The joint committee has power to make regulations for prescribing standards, tests, adding to the Schedule, prescribing the forms of licences, including inspection of premises and plant, and to take samples, and to exclude any substance used solely for veterinary purposes. If advertised or sold as a proprietary medicine or contained in such medicine, such accepted scientific name, or name descriptive of the true nature and origin of the substance, as may be prescribed, shall appear on the label. Date of manufacture shall be stated on all vessels or packages, and the sale is prohibited after the expiry of the prescribed period.
6. Contravention of the Act renders a person liable on summary conviction to a fine not exceeding £100, and on second or subsequent convictions to a fine and imprisonment, with or without hard labour for not exceeding three months, and in either case goods to be forfeited and licence may be revoked or suspended.
7. (1) The licensing authorities are for England and Wales, the Minister of Health; for Scotland, the Scottish Board of Health; for Northern Ireland, the Minister of Home Affairs for Northern Ireland.

### THERAPEUTIC SUBSTANCES REGULATIONS, 1931, SUMMARISED.

*With the amendments of subsequent regulations (S.R. & O. 1935, No. 580; S.R. & O. 1937, No. 767; S.R. & O. 1939, No. 1395) incorporated.*

**PART I. Interpretation; revocation of Regulations; addition of sterilised surgical ligature and suture as substances to which the Act of 1925 applies; licences and applications for licences.**

**PART II. Licences for manufacture of therapeutic substances.**

6. Applicant to satisfy the licensing authority that upon issue or renewal of licence the conditions set out in No. 7 of these Regulations will be observed.
7. (a) Concerns provision of adequate staff and premises for manufacture. (amended by S.R. & O. 1939, No. 1395).
- (b) And for tests of the strength, quality and purity of the substance, including housing for animals used, the licensee shall maintain staff and premises to carry out tests, or make arrangements with some institution approved for such tests to be regularly carried out on his behalf.
- (c) Records of manufacture and tests to be kept with batch-number.
- (d) Inspectors may inspect the premises and plant, and the process of manufacture and the means employed for standardising and testing, and may take samples.
- (e) Any changes in the expert staff responsible and in the premises or plant to be reported.
- (f) Samples to be furnished on request.
- (g and h) Batches may be withheld from sale.
- (i) Licensee to comply with Parts III and IV and further requirements if necessary.

**PART III. Provisions with regard to names of substances and to containers, etc.**

8. *Name of Substance.*—If any substance is advertised or sold as a proprietary medicine, or is contained in a medicine the "proper name" of the substance shall appear on the label in the manner prescribed in this Part of these Regulations.
9. *Containers.*—The substance is to be sealed in a previously sterilised glass container. (Ligatures and sutures may be in containers other than glass.)
10. *Labelling.*—The following are required on every sealed container:—
  - (a) The proper name of the substance in letters not less conspicuous than those in which the proprietary name, if any, is written or printed, and following immediately after or under such proprietary name.
  - (b) The number of the licence under which the substance is manufactured preceded, in the case of import licences, by the words "Import Licence."
  - (c) A distinctive batch-number.
  - (d) Where a test for potency in units is required by these Regulations, a statement of the potency in units defined in terms of relation to the standard preparation described under these Regulations. (This does not apply to vaccine lymph or surgical ligature or suture.) In addition to the above, the following particulars together with any others specified in the relative schedule must appear either on the label on the container or on a label or wrapper affixed to any package in which the container is issued for sale:—
  - (e) The name and address of the maker, date of manufacture, and statements of toxicity if required, nature of antiseptic if any, are also enforced, also date of removal from cold storage at a temperature not exceeding 5°C.
11. The sale of a substance after prescribed date is prohibited, but a doctor may override this, if his attention has been drawn to the date and he is satisfied it is required by the urgency of the case.

**PART IV. Standards of strength, quality and purity, and tests for determining.**

15. Tests for living aerobic or anaerobic bacteria are to be made in the case of:—

- (a) Sera and solutions of serum proteins for injection.
  - (b) Certain bacterial vaccines (anti-typhoid, anti-typhoid-paratyphoid (T.A.B.), anti-typhoid-paratyphoid-cholera (T.A.B.C.), anti-plague, anti-dysentery, and whooping-cough vaccines).
  - (c) Toxins, antigens, and mixtures of toxins or antigens with serum which are intended to be used in medical practice for immunising treatment, or for diagnosis by inoculation of the patient.
  - (d) Solutions of insulin.
  - (e) Dry preparations of insulin intended for therapeutic use.
  - (f) Preparations of the posterior lobe of the pituitary body intended for use by injection, except preparations which, after being sealed in the containers, have been sterilised by heat in a manner satisfactory to the licensing authority.
16. The tests are to be applied:—
- (a) To samples taken from each batch of the substance before filling and sealing the containers; and
  - (b) To the contents of sample containers when ready for issue.
17. (a) In the case of samples taken from the batch at the time when the test is made, the quantity taken for test shall be not less than 0.1% of the total volume of the batch if the volume is not more than 10 litres, and not less than 10 Cc. if the volume is 10 litres or more, but shall in no case be less than 1 Cc. If the batch is contained in a number of bulk containers, samples in these proportions shall be taken from each of such bulk containers and separately tested.
- (b) In the case of the contents of sample containers, the number shall be not less than 1% of the total filled from the batch, if this number is not more than 1000, and not less than 10 if the total number is more than 1000.
18. Defines method of preparing and using media.
19. (1) In the case of samples taken from the batch, one-half of the total volume of the sample is to be used for aerobic and one-half for the anaerobic test.
- (2) In the case of the contents of sample containers, the contents of each container shall be tested for aerobic and anaerobic organisms. When the volume in each container is 2 Cc. or more, 1 Cc. shall be used for each test. When the volume in the container is less than 2 Cc., the contents shall be divided into two approximately equal parts, one for the aerobic and the other for the anaerobic test.
- (3) The inoculated tubes shall be incubated at 37°C. for five days and examined after incubation, permanent records being kept of such examination of each tube.
20. (1) If at this examination no growth is found in any tube, the sample has passed the test.
- (2) If at the examination a growth is visible, further samples may be taken and the tests repeated. The taking of samples from the batch may, if necessary, be repeated twice. If the same organism is visible in more than one test, the batch shall be treated as not sterile, and the material contained in the batch shall not be issued or used as part of a further batch unless and until it has been re-sterilised and has passed the tests.
21. Emergency Regulations.
22. Freedom from abnormal toxicity is ensured by injecting 0.5 Cc. of the serum into a normal mouse, and 5 Cc. into a normal guinea-pig.

#### PART V. Licences for import of substances.

23 and 24.—Broadly, the applicant must furnish a written undertaking signed by, or on behalf of, the manufacturer that the manufacturer will comply with the Regulations as to manufacture and testing.

PART VI. 25. Research Licences. Special modifications apply.

PART VII. 26. Substances manufactured or imported for export only. The licensing authorities may dispense with any of the requirements of the Regulations, if necessary.

#### PART VIII. Substances for veterinary use only.

27. Containers to be marked "to be used solely for veterinary purposes."

**PART IX. Non-sterile Surgical Ligatures and Suture.**

28. Containers and wrappers must be labelled in red ink "non-sterile surgical ligature (suture)—not to be used for operations upon the human body unless efficiently sterilised."

**FIRST SCHEDULE** provides forms of application for, and grant of, licences.

**SECOND SCHEDULE, PART I. Vaccines, toxins, antigens, sera and antitoxins.**

(A) Provisions applicable to the production of bacterial vaccines.

(1) Defines a bacterial vaccine.

(2) Requirements in respect of the staff of manufacturer.

(3) The proper name of a vaccine is the name of the micro-organism followed by the word "vaccine," except in the following:—

Anti-typhoid vaccine, anti-typhoid-paratyphoid vaccine (T.A.B.), anti-typhoid-paratyphoid A, B and C vaccine, anti-typhoid-paratyphoid cholera vaccine A and B, and anti-plague vaccine, whooping-cough vaccine, anti-dysentery vaccine (as amended 1941).

(6) The label on the container must indicate composition:—

(a) Number of micro-organisms per Cc. or

(b) Weight of dried substance of micro-organisms per Cc. or

(c) Number of micro-organisms or weight of dried substance of organisms used in preparing 1 Cc. of the finished product.

(B) Special provisions for Vaccine Lymph (Vaccinia).

(1) The proper name is "Vaccine Lymph."

Staff of establishment, housing of animals, precautions to observe, containers, labelling, tests for purity (glycerination and cold storage, tests of gas-producing anaerobic organisms, living hæmolytic streptococci) and potency are included.

**PART II. Toxins and antigens.**

(A) Provisions applicable to reagents used in the Schick Test for the diagnosis of susceptibility to diphtheria.

1.—(1) The reagents used in the Schick Test are two, Schick Toxin and Schick Control. Their proper names respectively are "Schick Test Toxin" and "Schick Control."

(2) Schick Toxin is a sterile filtrate from a culture on nutrient broth of the specific organism of diphtheria (*Corynebacterium diphtherie*). It may be issued either (i) undiluted, or (ii) already diluted with saline solution to the strength proper for use in the test.

(3) Schick Control is prepared from the same batch of Schick Toxin as that with which it is issued for sale, by destroying the specific toxicity at 70°C. for a time not shorter than 5 minutes.

2. Tests for potency.

(B) Provisions for Diphtheria Prophylactic (amended by S.R. & O. 1935, No. 580).

(C) Provisions for Tuberculin and other preparations from the bacillus tuberculosis and its cultures.

The following has been added by S.R. & O. 1935, No. 580:—

(D) Provisions for Staphylococcus toxoid.

The following has been added by S.R. & O. 1939, No. 1395:—

(E) Provisions for Tetanus toxoid.

**PART III. Provisions applicable to production of all sera from living animals.****PART IV. Provisions for particular sera and antitoxins.**

(A) Anti-bacterial sera and anti-toxic sera for which no potency test is prescribed.

(B) Anti-dysentery serum (Shiga) and other anti-dysentery sera.

(C) Diphtheria antitoxin.

(D) Tetanus antitoxin.

(E) Gas-gangrene antitoxin (perfringens).

The following have been added by S.R. & O. 1935, No. 580:—

(F) Antipneumococcus serum (Type I).

(G) Antipneumococcus serum (Type II).

(H) Staphylococcus antitoxin.

(I) Gas-gangrene antitoxin (oedematiens).

(J) Gas-gangrene antitoxin (vibrio septique).

The following has been added by S.R. & O. 1939, No. 1395:—

(K) Gas-gangrene antitoxin (histolyticus).



**THIRD SCHEDULE. Arsphenamine and derivatives.**

**PART I.** General provisions applicable to arsphenamine and derivatives. The standard preparations are kept in the National Institute for Medical Research, Hampstead. Biological tests are applied and tests for maximum toxicity and for therapeutic potency.

**PART II.** Special provisions for arsphenamine. Chemical and physical.

**PART III.** Special provisions for neo-arsphenamine.

**PART IV.** Special provisions for sulpharsphenamine.

**PART V.** Special provisions for derivatives of arsphenamine other than neo-arsphenamine and sulpharsphenamine.

**FOURTH SCHEDULE. Insulin.**—Proper name. Special conditions of licence. Standard. Units. Quality. Tests. Container. Label.

**FIFTH SCHEDULE. Pituitary (Posterior Lobe) Extract.**—Proper name. Standard. Units. Quality. Tests. Container. Label.

**SIXTH SCHEDULE. Sterilised Surgical Ligature and Suture.**—Proper name. Tests for sterility. Label. (Amended by S.R. & O. 1937, No. 767.)

**EMERGENCY POWERS (DEFENCE) (SHORTAGE OF DRUGS)  
ORDER, SUMMARISED.**

MADE UNDER REGULATION 60H OF THE DEFENCE (GENERAL) REGULATIONS, 1939.  
—S.R. & O. 1941, No. 273 (Feb. 24, 1941).

1. Any person dispensing or supplying medicines on prescriptions requiring the use or supply of a quantity of a substance set out in the first column of the Schedule to this order (in this order referred to as a "scarce substance") may use or supply the corresponding amount of the authorised alternative, unless the prescription expressly forbids the use or supply of another substance by the insertion against the scarce substance of the letters "N.A." or of words indicating that no other substance is to be used or supplied in place of the scarce substance.
2. The "authorised alternative" to a scarce substance is the substance set out in relation to the scarce substance in the second column of the Schedule to this order, and equal quantities of the scarce substance and of the authorised alternative are deemed to correspond.

**SCHEDULE**

Scarce substance	Authorised alternative
Potassium bicarbonate .. ..	Sodium bicarbonate
Potassium bromide .. ..	Sodium bromide
Potassium citrate .. ..	Sodium citrate
Potassium iodide .. ..	Sodium iodide

## THERAPEUTIC INDEX OF DISEASES AND SYMPTOMS

This index is included as a general guide to treatment by drugs and is intended to refer the reader to the text, the number following each entry indicating the page or pages on which information may be found concerning the use of the drug in the disease under consideration (*see also* Preface, p. xxiv).

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**Local.**—Tinct. Benz. Co. (inhalation), 30; Æthyl. Iod. (inhalation), 152; Lin. Capsic., 361; Cocain., 422; Lin. Succin. Co., 454; Creosot., 460; Ferr. Perchlor., 527; Liq. Hydrog. Perox., 612; Iodum, 645; Menthol, 695; Ol. Eucalypt., 742; Tereben., 830; Sod. Bicarb., 919; Thymol, 989.

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**Bruises. Local.**—Anthem. (as a fomentation), 187; Tinct. Arnica. Flor., 362; Tinct. Arnica. Rad., 363; Tinct. Calend., 363; Hamam., 564; Mag. Sulph., 684; Liq. Plumb. Subacet. Dil., 856; Lot. Plumb. Evap., 857.

**Burns, Acute Toxæmia of.**—Ext. Suprarenal. Cort., 140; Desoxycorticosterone Acetate, 143; Dextros. (intrav. or rectal), 475. See also Shock.

**Burns and Scalds.**—Benzoyl. Perox., 31; Amyl. Salicyl., 103; Acid. Tann., 112; Liq. Ammon. Tart., 117 (eye); Acriflavin., 125; Eufavin., 127; Kaolin., 175; Argent. Nit., 204; Viola Cryst., 255; Liq. Tinct., 258; Bism. Subgall., 312; Lin. Calc. Hydrox. c. Ol. Lini, 341; Trichlorethylent., 372 (tar burns); Chlorbutol, 393; Cocain., 422; Benzocain., 429; Mercurochrom., 606; Zinc. Perox., 615; Ichtham., 621; Ol. Eucalypt., 742; Ol. Morr., 754; Ung. Ol. Ricin. Co., 763; Oxygen. (injections), 773; Paraff. Dur., 781; Albumen, 798; Ol. Carbol., 811; Lead Lotions, 856; Sod. Bicarb., 919; Sulphanilamid., 952; Thymol. Iod., 990; Trinitrophen., 1004; Zinc Oxid., 1015. See also Mustard Gas Burns.

**Calculi, Biliary.**—Benzyl. Benz., 30; Borax, 37; Acid. Oleic., 86; Sod. Salicyl., 98; Æther, 146; Amyl. Nitris (inhaled), 161; Ephed., 494; Bile Salts, 518; Hexamin., 582 et seq.; Morph., 701; Papaverin. Sulph., 708; Ol. Oliv., 761; Opium, 766; Papaveret., 769; Pilocarp., 823; Podoph. Res., 858; Sod. Oleas, 907; Sp. Æther. Nitros., 924.

**Calculi, Urinary.**—Pot. Chlorid., 62; Sod. Phosph. Acid., 93; Bellad. Fol., 289; Ammi Vismaga, 320; Piperaz., 365; Hexamin., 582; Papaverin. Sulph., 708; Pot. Bicarb., 862; Sp. Æther. Nitros., 924; Dilute Mineral Acid.

**Cancer.**—Inj. Sod. o-Coumarat., 32; Alcohol (injection), 157; Fluorescein. Solub., 816; Colloidal Lead, 858; Sod. Oleas, 907; Cobra Venom, 1069; Radium and X-rays, Vol. II.

**Cancrum Oris.**—See Stomatitis.

**Carbuncles.**—See Boils and Carbuncles.

**Caries. Local.**—Past. Arsen., 212; Creosot., 460; Collod. Carbol., 809.

**Internal.**—Vitamin D, 329.

- Cataract.**—Acid. Ascorb., 22; Senecio, 560.  
**Catarrh, Bronchial.**—See Bronchitis.  
**Catarrh, Gastric.**—Bism. Salicyl., 310; Ferr. et Ammon. Cit., 523; Hydrast., 609; Ichtham., 621.  
*Local.*—Acid. Boric., 34; Sod. Bicarb., 919.  
**Catarrh, Gastro-intestinal.**—See Gastritis.  
**Catarrh, Nasal.**—Sod. Sulphanilic., 6; Calc. Acetylsalicyl., 18; Neb. Benzoin. Co., 30; Mag. Thiosulph., 109; Adrenal. (in a spray), 134; Atrop., 238; Insuff. Bism. et Morph., 313; Camph., 343; Carbon Diox., 368; Ol. Cinnam. (inhaled), 418; Neb. Cocain., 422; Cubeb., 457; Ephed. (in a spray), 494; Amphetamina (inhaled), 499; Euphorb., 503; Mucin, 579; Hydrast., 609; Syr. Iodotann., 650; Pulv. Ipecac. et Opii, 658; Menthol, 695; Ol. Eucalypt. (inhaled), 742; Ol. Menth. Pip., 744; Phenazon. Salicyl., 804; Phenol, 808; Ol. Pini Pumil. (inhaled), 830; Ol. Pic. (inhaled), 851; Quinin. (and salts), 873; Sod. Bicarb. (local), 919; Sulphanilamid., 943 *et seq.*; Thymol, 989; Anti-Catarrhal Vaccines, 1032; Oral Cold Vaccine, 1034.  
**Catarrh, Spring.**—Acid. Acet. Dil., 8; Quinin. Bisulph., 876.  
**Catarrh, Uterine.** *Local.*—Argent. Picras. (and other Silver Salts), 206; Glycer., 552; Glycer. Plumb. Subacet., 856; Zinc. Sulph., 1018.  
**Catarrh, Vesical.**—See Cystitis.  
**Cellulitis.**—Iodum, 646; Sulphanilamid., 943 *et seq.*; Sulphathiazol., 971.  
*Local.*—Glycer., 552; Mag. Sulph., 684; Mag. Sulph. and Ethylene Glycol Paste, 687.  
**Cerebrospinal Fever.**—See Meningitis.  
**Cervicitis.**—Mercurochrom., 606; Ichtham., 621; Electrotherapy, Vol. II.  
**Chancres, Soft.**—Arsphenamin., 227; Neosarsphenamin., 230.  
*Local.*—Bism. Oxyiodogall., 309; Pyrogall., 868; Resorcin., 895. *See also Syphilis.*  
**Chancroid.**—Antim. et Pot. Tart., 196; Sulphanilamid., 943 *et seq.*; Sulphapyridin., 961 *et seq.*  
*Local.*—Bism. Benz., 300; Iodof., 640.  
**Cheyne-Stokes' Respiration.**—Histam. Phosph. Acid., 511; Theophyll. c. Æthylenediamin., 987.  
**Chilblains.**—Calc. Chlorid., 60; Calc. Lact., 76; Calc. et Sod. Lact., 77; Calc. Glucon., 339; Ext. Parathyroid., 1001; Ultra-violet Light, Vol. II; Electrotherapy, Vol. II.  
*Local.*—Calc. Iod., 48; Collod. Atrop., 240; Capsic., 362; Ung. Calc. Chlorinat., 398; Glycer., 552; Liq. Iod. Decol., 648; Ung. Rusc. Co., 854; Calamin., 1019.  
**Chloasma.**—Acid. Sulphuros., 109; Sod. Thiosulph., 110.  
 (The following lotion is advocated by Chopra: Mercuric chloride, 1 to 2 gr., bismuth subnitrate 10 gr., tragacanth powder, 5 gr., water 1 oz.; to be painted on dark patches.)  
**Chlorosis.**—See **Anæmia, Secondary.**  
**Cholangitis.**—Ext. Fel. Bov., 517.  
**Cholecystitis.**—Bile Salts, 518; Hexamin., 582; Mag. Sulph., 684; Ol. Oliv., 761; Curcumin, 1021.  
**Cholelithiasis.**—See **Calculi, Biliary.**  
**Cholera.**—Hypertonic Saline, 67; Acid. Sulph. Aromat., 105; Acid. Sulph. Dil., 106; Acid. Sulphuros., 109; Ol. Allii, 167; Kaolin., 175; Betanaph., 297; Mist. Cret. Co., 338; Cupr. Sulph., 471; Pot. Permang., 692; Morph., 701; Opium, 768; Papaveret., 769; Bism. Tribromphen., 815; Plumb. Acet., 856; Anti-Cholera Vaccine, 1037; Cholera Bacteriophage, 1037.  
 (Tomb's Essential Oil Mixture.—Aniseed oil, cajuput oil, juniper oil, of each 5 m., aromatic sulphuric acid 15 m., spirit of ether 30 m.;  $\frac{1}{2}$  dr. in an ounce of water every 15 minutes for 2 or 3 hours.)  
**Chordee.**—Bromides, 55; Bellad. Rad., 291; Camph., 343; Camph. Monobrom., 346; Cannab., 354.  
**Chorea.**—Acid. Acetylsalicyl. (and salts), 16; Acetyl-para-amidosalol, 21; Calc. Chlorid., 60; Bulbocapnine, 123; Argent. Oxid., 205; Arsen. Trioxid., 211; Sod. Cacodyl., 216; Phenylethylhydantoin, 286; Bromal Hydr., 315; Camph. Monobrom., 346; Cannab., 354; Chloral Hyd., 391; Chlorbutol, 393; Conium, 454; Visc., 456; Gelsem., 546; Cimicif., 549; Hexamin., 583; Hyosc. Hydrobrom., 618; Mag. Sulph., 685; Non-specific Vaccines, 794; Phenazon., 802.  
**Cicatrical Tissue.**—Inj. Thiosinamin. et Sod. Salicyl., 917; Thiosinamin. et Æthyl. Iod., 918.

**Claudication, Intermittent.**—Acetylcholine, 12; Carbachol, 13; Acetyl- $\beta$ -methylcholine Chloride, 14; Tissue Extracts, 580.

**Cold, Common.**—See *Catarrh, Nasal*.

**Colic, Biliary.**—See *Calculi, Biliary*.

**Colic, Intestinal.**—Benzyl. Benz., 30; Bellad. Fol., 289; Cannab., 354; Carum, 375; Chlorof., 401; Tinct. Chlorof. et Morph., 405; Hyoscy., 616; Ol. Cajuput., 740; Ol. Lavand., 744; Ol. Menth. Pip., 744; Ol. Ricin., 763; Opium, 766; Papaveret., 769; Physostig., 820; Stramon., 925; Zingib., 1021.

**Colic, Lead.**—Acid. Sulph. Dil., 106; Chlorof. (inhaled), 401; Tinct. Chlorof. et Morph., 405; Erythrityl. Tetranit., 515; Morph., 701; Opium, 766; Papaveret., 769; Ext. Parathyroid., 1000.

**Colic, Renal.**—Benzyl. Benz., 30; Amyl. Nitris (inhaled), 161; Atrop., 238; Bellad. Fol., 289; Chlorof. (inhaled), 401; Ephed., 494; Hyoscy., 616; Morph., 701; Opium, 766; Papaveret., 769; Stramon., 925.

**Colic, Uterine.**—Benzyl. Benz., 30.

**Colitis.**—Acid. Lact. Bacilli, 80; Ammon. Mandel., 83; Alumin. Hydrox., 174; Argentoprot., 207; Argent. Protein. Mit., 207; Methylthionin. Chlor., 258; Enema Bism. et Sod. Salicyl., 313; Hexamin. Salicyl., 584; Iodum, 644; Ol. Oliv., 761; Oxygen., 773; Polyvalent Antidysentery Serum, 1048.

**Colitis, Mucous.**—Acid. Lact. Bacilli, 80; Ammon. Mandel., 83; Enema Bism. et Sod. Salicyl., 313; Hexamin. Salicyl., 584; Ol. Oliv., 761; Sod. Bicarb., 919; B. Coli Vaccine, 1038.

*Per rectum.*—Daily irrigations with warm Normal Saline Solution; Enema Ol. Oliv., 761; Oxygen., 773.

**Colitis, Ulcerative.**—Alumin. Hydrox., 174; Bism. Subgall., 312; Ol.; Morr., 755; Tinct. Opii, 766; Polyvalent Anti-Dysentery Serum, 1048.

*Per rectum.*—Liq. Sod. Chlorid. Physiol., 65; Alumin. Hydrox., 174; Argent. Protein. Mit., 207; Methylthionin. Chlor., 258; Enema Opii, 766.

**Collapse and Fainting.**—Adrenal., 135; Pholedrine, 138; Ether, 146. Alcohol, 157; Ammon. Carb., 179; Sp. Ammon. Aromat., 179; Caffeine et Sod. Benz., 323; Camph., 343; Sod. Camphorsulphon., 346; Leptazol, 348; Nikethamid., 350; Digitalin., 485; Ephed., 494; Histam. Phosph. Acid., 511; Nitroglycer., 711; Ext. Pituit. Liq., 833; Strych., 930. See also *Shock*.

**Coma, Diabetic.**—Inj. Sod. Chlorid. et Acac., 1; Liq. Sod. Chlorid. Physiol., 66; Insulin, 631; Sod. Bicarb., 920.

**Conjunctivitis.**—Acid. Boric., 35; Acriflavin., 125; Eusflavin., 127; Proflavin., 129; Argent. Iod., 203; Argent. Nit., 204; Argentoprot., 206; Argent. Protein. Mit., 207; Aur. et Sod. Chlorid., 248; Viola Cryst., 256; Methylthionin. Chlor., 258; Cupr. Sulph., 471; Hydrarg. Cyanid., 590; Oculent. Flav., 596; Ung. Hydrarg. Oxid. Flav., 596; Hydrarg. Oxycyanid., 597; Mercuriochrom., 606; Liq. Hydrog. Perox., 612; Ichtham., 622; Iodum, 644; Ol. Morr., 755; Ol. Ricin., 763; Quinin. Bisulph., 876; Ethylhydrocuprein. Hydrochlor., 894; Resorcin., 895; Sulphapyridin., 961 *et seq.*; Zinc. Chlorid., 1014; Zinc. Sulph., 1018.

**Constipation. (Cholagogues).**—Sod. Salicyl., 98; Euonym., 516; Ext. Fel. Bov., 517; Sod. Tauroglycochol., 517; Dehydrocholic Acid, 518; Hydrarg., 587; Ext. Hydrast., 609; Mag. Sulph., 684; Podoph. Res., 858; Tarax., 900; Sod. Oleas, 907.

*(By hypodermic injection).*—Physostig., 820; Prostigmin, 821; Ext. Pituit. Liq., 833.

*(Laxatives).*—Sod. Chlorid., 64; Acid. Lact. Bacilli, 80; Agar, 154; Casc. Sagr., 376; Cerevis. Ferment., 384; Cass. Fruct., 418; Glycer., 552; Pulv. Glycyrrh. Co., 557; Marrub., 558; Ispagh., 677; Psyllium, 677; Ol. Oliv., 761; Paraff. Liq., 782; Phenolphthal., 815; Rheum, 898; Sap. Moil., 906; Senna, 914; Baptisia, 915; Ficus, 915; Tamarind., 916; Sulphur, 974.

*(Purgatives).*—Sod. Chlorid., 64; Sod. Sulph., 106; Aloe., 168; Aloin., 169; Apocyn., 355; Colocynth., 450; Hydrarg., 587; Hydrarg. Subchlor., 603; Jalap., 666; Ipom., 667; Cambog., 667; Kalad., 667; Scammon. Res., 667; Leptand., 668; Turpeth., 668; Mag. Sulph., 684; Ol. Ricin., 763; Ol. Croton., 764; Phenolphthal., 815; Podoph. Res., 858; Senn. Fruct., 914.

*(Per rectum).*—Fel. Bov., 517; Glycer., 552; Ol. Oliv., 761; Enema Sap., 906.

*(Saline aperients).*—Mag. Chlorid., 62; Sod. Chlorid., 64; Sod. Phosph., 93; Pot. Sulph., 106; Pot. Tart. Acid., 118; Pulv. Efferv. Co., 119; Sod. et Pot. Tart., 119; Mag. Carb. Lev. *vel* Fond., 681; Mag. Hydrox., 682; Mag. Oxid. Lev. *vel* Fond., 683.

**Convulsions.**—Pot. Brom., 55; Sod. Brom., 57; Amyl. Nitris, 160; Barbiturates, 264; Amytal, 273; Calc. Glucon., 339; Camph. Monobrom., 346; Mosch., 352; Chloral Hydr., 391; Chlorof., 401; Hyoscin. Hydrobrom., 618; Morph., 701. *See also Anesthesia, to produce.*

**Cornea, Inflammation and Ulcers of.**—Acid. Boric., 35; Argent. Iod., 203; Argentoprot., 206; Argent. Protein. Mit., 207; Atrop., 242; Oculent. Atrop. c. Hydrarg. Oxid., 242; Homatrop. Hydrobrom., 244; Rub. Scarlet., 260; Vitamin A, 334; Carbon Dioxide Snow, 368; Hydrarg. Perchlor., 599; Mercurochrom., 606; Iodum, 644; Æthylmorph. Hydrochlor., 704; Ol. Morr., 754; Physostig., 820; Quinin., 874; Lot. Quinin. Hydrochlor., 879; Quinin. Sulph., 885; Æthylhydrocuprein. Hydrochlor., 894.

**Corns.**—*See Warts.*

**Coryza.**—*See Catarrh, Nasal.*

**Cough.**—Acid. Hydrobrom. Dil., 52; Troch. Ammon. Chlor., 60; Acid. Hydrocyan. Dil., 71; Agar, 154; Chondrus, 154; Allyl. Sulphid., 168; Ammon. Carb., 179; Apomorph. Hydrochlor., 202; Bals. Tolu., 263; Camph., 343; Chlorof., 401; Codein. (and salts), 442; Dicotid., 444; Dilaudid., 444; Ol. Santal., 458; Creosot., 460; Glycer., 552; Glycyrrh., 556; Althæa, 558; Marrub., 558; Tussilag. Flos., 559; Lactuc., 621; Ipecac., 656; Linum, 676; Morph., 700; Æthylmorph. Hydrochlor., 704; Diamorph. Hydrochlor., 705; Opium, 766; Papaveret., 769; Pinus, 827; Terebin., 830; Terpin. Hydr., 831; Pix Liq., 851; Scilla, 911; Seneg., 912; Cocill., 913; Prun. Serot., 913.

**Cretinism.**—Thyroid., 994; Thyroxinsod., 997.

**Croup.**—Calc. Glucon., 339; Chlorof., 401; Ipecac., 656.

**Croup, False.**—*See Laryngismus Stridulus.*

**Cryptorchidism.**—Androgens, 734 *et seq.*; Gonadotrophic Factor, 843.

**Cushing's Syndrome.**—Estron., 723.

**Cystitis.**—Ammon. Benz., 28; Sod. Benz., 29; Citrates, 40; Acid. Lact., 75; Acid. Mandel. (and salts), 82; Sod. Phosph. Acid., 93; Salicyl. Salicyl., 103; Argent. Nit., 204; Argent. Protein. Mit., 207; Methylthionin. Chlor., 258; Betanaphthyl. Salicyl., 298; Buchu, 319; Maidis Stig., 321; Uva Ursi, 321; Acid. Camph., 346; Codein., 442; Ol. Santal., 458; Sabal, 459; Hexamin., 582 *et seq.*; Mercurochrom., 605; Ol. Terebinth., 828; Pot. Bicar., 862; Hexyl-resorcin., 897; Sod. Bicar., 919; Sulphanilamid., 949; Sulphathiazol., 970.

**Local.**—Liq. Calc. Chlorinat. c. Acid. Boric., 398; Quinin. Bisulph., 876; Resorcin., 895. *See also Urinary Tract Infections.*

**Debility.**—Acid. Phosph. Dil., 90; Aneurin. Hydrochlor., 190; Arsen. Trioxid., 211; Calc. Glucon., 339; Cinchona preparations, 413; Iron preparations, 521; Gentian., 547; Calumb., 548; Insulin, 632; Ext. Malt. and preparations, 687; Nux Vom., 712; Ol. Morr., 754; Quinin., 873; Ferr. et Quinin. Cit., 877; Strych., 930; Thyroid., 994. *See also Neurasthenia.*

**Delirium Tremens.**—Sod. Brom. and other Bromides, 57; Ammon. Acet., 181; Acid. Nicotin., 193; Hexobarbiton. Solub., 277; Camph. Monobrom., 346; Cannab., 354; Chloral Hydr., 391; Paraldehyd., 540; Hyoscyamin. Sulph., 617; Hyoscin. Hydrobrom., 618. *See also Alcoholism, Acute.*

**Dementia Præcox.**—Mang. Chlorid., 691; Sulphur, 975.

**Dermatitis.**—Acid. Ascorb., 22; Sod. Thiosulph., 110; Calc. Thiosulph., 111; Nicotinic Acid Amide, 193; Viola Cryst., 257; Vitamins A and D, 329; Ichtham., 621; Sod. Bicar., 919.

**Local.**—Ung. Acid. Salicyl., 95; Liq. Sod. Chlorinat. Chir., 400; Ext. Grindel. Liq., 664; Pot. Permang., 692; Gelat. Zinc., 1015; Ung. Zinc. Oxid., 1017; Lot. Calamin., 1019; Titani Oxid., 1021.

**Dhobie's Itch.**—Liq. Calc. Sulphur., 342; Iodum, 644; Ung. Resorcin. et Acid. Salicyl., 896.

**Diabetes Insipidus.**—Ext. Pituit. Liq., 833; Pituitary (Posterior Lobe), 849.

**Diabetes Mellitus.**—Liq. Pot. Arsen. et Brom., 213; Diabetic Foods, 383; Codein., 442; Insulin., 630; Protamine Insulinate, 635; Protamine Zinc Insulin, 635; Oral Diabetic Preparations, 638-9; Ovocleithin., 771.

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**Local.**—Borax, 37; Acid. Iodic., 52; Acid. Lact., 75; Acid. Sulphuros., 109; Acid. Malic., 119; Alcohol, 157; Argent. Colloid., 208; Formaldehyd., 536; Hydrarg. Cyanid., 590; Lot. Hydrarg. Biniod. Spirit., 593; Liq. Hydrog. Perox., 612; Pig. Menthol. et Toluen., 696.

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**Dropsy, Cardiac.**—Asparagin, 44; Caffein., 322; Caffein. et Sod. Iod., 324; Apocyn., 355; Canthar., 386; Elaterium, 451; Scopar., 455; Spart. Sulph., 456; Digit., 481; Pil. Digit. Co., 484; Digitalin and other glycosides, 485 *et seq.*; Pil. Hydrarg., 588; Mersaly., 608; Scilla, 911; Strophanth., 927; Strophanthin., 927; Theobrom. (and salts), 984; Theophyll. (and salts), 985; Urea, 1006. *See also Heart Disease.*

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**Dropsy, Renal.**—Pot. Acet., 8; Sod. Acet., 9; Pot. Tart. Acid., 118; Sod. et Pot. Tart., 119; Elaterium, 451; Lactos., 477; Mersaly., 608; Pulv. Jalap. Co., 666; Pilocarp., 823; Theophyll. (and salts), 985. *See also Nephritis.*

**Dupuytren's Contraction.**—Inj. Thiosinam. et Sod. Salicyl., 917; Thiosinam. et Æthyl. Iod., 918.

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**Dysentery, Bacillary.**—Benzyl. Benz., 30; Sod. Sulph., 106; Argent. Nitras, 204; Argent. Oxid., 205; Argentoprot., 207; Argent. Protein. Mit., 207; Silver Gelatose, 208; Bism. Carb., 301; Bism. Subgall., 312; Creosot., 460; Hexamin. Salicyl., 584; Ulm. Fulv., 678; Pot. Permang., 692; Ol. Ricin., 763; Rheum, 898; Bacteriophage, 1026; Serum Antidysenteric. (Shiga), 1047; Antidysentery Vaccine, 1048.

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**Eclampsia.**—Calc. Chlorid., 60; Apomorph. Hydrochlor., 202; Calc. Glucon., 339; Verat. Vir., 364; Chloral Hydr., 391; Insulin., 633; Mag. Sulph., 685; Morph., 701; Papaverin. Sulph., 708; Pilocarp., 823; Theophyll. c. Æthylendiamin., 987; Parathyroid, 1000.

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*Local.*—Oleat. Brom. (intrav.), 57; Ung. Plumb. Oleat., 88; Ung. Zinc. Oleas., 89; Zinc. Oleostear., 89; Ung. Acid. Salicyl., 95; Sod. Thiosulph., 110; Acid. Tann., 112; Acriflavin., 125; Amyl. Nitris., 161; Alum., 171; Cataplasma. Amyli., 185; Argent. Nit., 204; Arsen. Trioxid., 211; Sod. Arsen. Anhydros., 214; Sod. Cacodyl., 216; Viola Cryst., 257; Methylthionin. Chlor., 258; Betanaph., 297; Glycer. Bism. Nit., 309; Bism. Subgall., 312; Liq. Calc. Sulphur., 342; Carbo., 367; Carbon Dioxide Snow, 368; Eugen., 374; Dithranol, 412; Cocain., 421; Benzocain., 428; Cupr. Sulph., 472; Formaldehyd., 536; Ung. Hydrarg. Ammon., 590; Ung. Hydrarg. Nit., 594-5; Ung. Hydrarg. Oxid. Flav., 596; Cotarn. Chlorid., 611; Ung. Hydrog. Perox., 614; Ichtham., 621; Estron., 723; Ol. Oliv., 761; Glycer. Papain., 780; Whole Blood Injections, 795; Phenol, 808; Pix Liq., 851; Ol. Pic., 851; Pix Carbon., 852; Past. Zinc. et Pic. Carbon., 853; Ol. Cadin., 853; Ung. Rusc. Co., 854; Glycer. Plumb. Subacet., 856; Pot. Carb., 862; Potass. Sulphur., 864; Pyrogall., 868; Resorcin., 895; Sod. Bicarb., 919; Sod. Carb., 921; Sulphur., 974; Thymol, 988; Thymol. Iod., 990; Trinitrophen., 1004; Zinc. Oxid., 1015; Calamin., 1019; X-rays and Ultra-Violet Light, Vol. II.

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**Endocarditis.**—Stront. Iod., 51; Pot. Salicyl., 97; Eufavin., 127; Argent. Colloid., 208; Sod. Cacodyl., 216; Viola Cryst., 255; Sulphanilamid., 943 *et seq.*; Sulphapyridin., 966; Serum Antistreptococcic., 1068; Vaccin. Streptococcic., 1068; Vaccin. Staphylococcic., 1073.

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Whale Oil .. .. .	761
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"    Germ Oil .. .. .	386 & V. II
"    Starch .. .. .	185 & V. II
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"    Apiol .. .. .	201
"    Arsenic .. .. .	209
"    Bryony .. .. .	122
"    of Egg .. .. .	798
"    Embrocation .. .. .	829
"    Hellebore Rhizome .. .. .	364
"    Indian Hemp Rhizome .. .. .	355
"    Lead .. .. .	857
"    Mustard .. .. .	916 & V. II
"    "    Seed Oil .. .. .	916
"    Oil of Camphor .. .. .	351
"    Pepper .. .. .	365 & V. II
"    Pine Bark .. .. .	827
"    Precipitate .. .. .	589 & V. II
"    "    (Fr. Cx.) .. .. .	602
"    Spirit .. .. .	786
"    Squill .. .. .	911
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"    Thyme Oil .. .. .	991
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Page	Line	
788	22	<i>delete</i> , consists of a partially phosphated (about 10%) cetyl-stearyl alcohol.
		<i>insert</i> . A wax-like homogeneous mixture of cetyl, stearyl or homologous fatty alcohols with approximately 10% of the sodium salts of the sulphated alcohols.
797	25	(from bottom) <i>for</i> <b>Pollacine</b> <i>read</i> <b>Pollaccine</b> .
816		(bottom line) <i>for</i> ( <i>Boots, Nottingham</i> ) <i>read</i> ( <i>British Drug Houses, London</i> ).
844	4	(from bottom) <i>delete</i> each containing 200 or 1000 rat units.
911	9	<i>for</i> <i>prescribed</i> <i>read</i> <i>supplied</i> .
929	21	<i>for</i> 1007 <i>read</i> 1107.
969	26	<i>for</i> intramuscular <i>read</i> intravenous.
	32	<i>for</i> 115 <i>read</i> 115° or 10.
999	29	<i>for</i> 1 = 5 <i>read</i> 1 = 10.
1011	4	<i>for</i> <i>prescribed</i> <i>read</i> <i>supplied</i> .
1078	6	<i>for</i> <b>Beranek's</b> <i>read</i> <b>Beraneck's</b> .

September 1942.

